

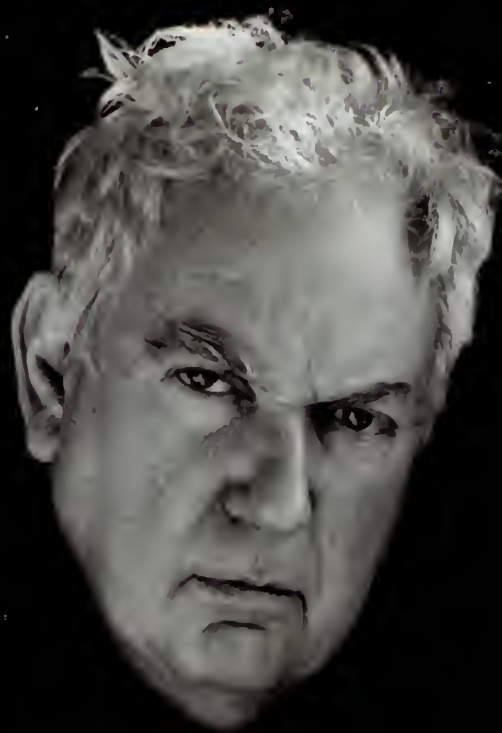
SPRING 2005

Harvard Medical

ALUMNI BULLETIN

HISTORY'S MEDICAL MYSTERIES

Did such artists as Alexander Calder craft their masterpieces with a blind eye? Was Julius Caesar the unwitting victim of assassins—or their puppeteer? And why did the grand admiral of the Dutch fleet suddenly keel over and die?





PIONEER

1967

The late A. Clifford Barger '43A spent 35 years researching the pathophysiology of congestive heart failure, renovascular hypertension, and coronary artery disease. The former Robert Henry Pfeiffer Professor of Physiology emeritus is remembered for his contributions to understanding the physiology of the heart and kidneys, but perhaps even more for his dedication to training scores of young investigators from under-represented minority backgrounds.

CONTENTS

DEPARTMENTS

Letters.....3

Pulse.....4

The Second Year Show lambastes the pharmaceutical industry; Match Day

Bookshelf.....8

Bookmark.....9

A review by Elissa Ely of *Seascapes*

President's Report.....10

by Joseph K. Hurd, Jr.

Editorial.....11

Was Michael Crichton irresponsible in writing a thriller that vilifies the environmental movement? by Eric Chivian

Benchmarks.....12

Cats and mice provide clues to a range of human diseases; treatment advances for brain tumors and heart attacks

Alumnus Profile.....56

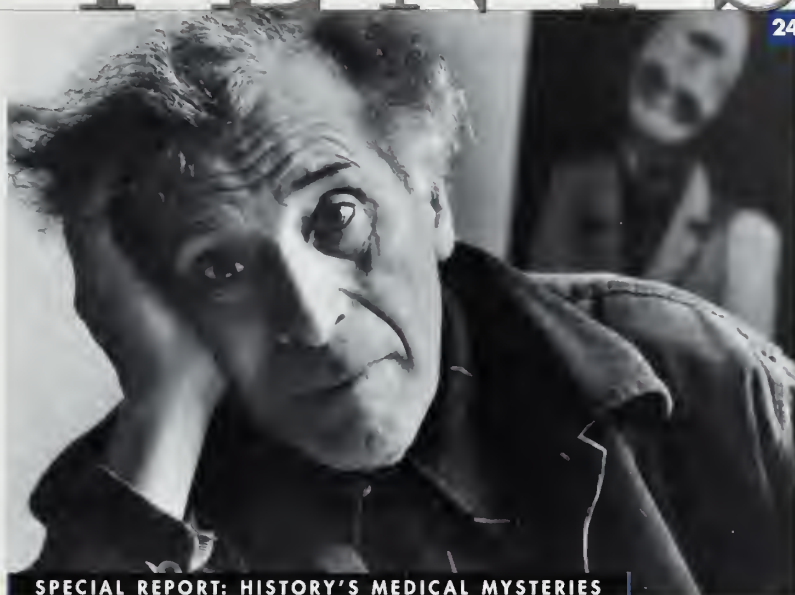
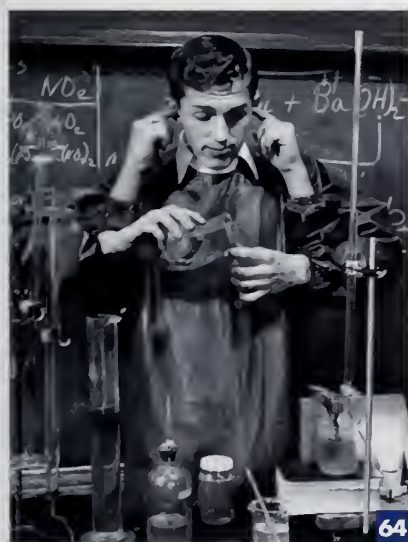
Orthopedic surgeon Bobby Satcher fulfills his boyhood dream of becoming an astronaut. by Janice O'Leary

Class Notes.....58

Obituaries.....61

Endnotes.....64

A practical joke leaves a chemistry student pondering his impending departure for the morgue. by William D. Cochran



SPECIAL REPORT: HISTORY'S MEDICAL MYSTERIES

Dead Men Talking.....16

Did Julius Caesar stage his own death? Was King Tut murdered? And what killed Alexander the Great? A forensic psychiatrist joins hot debates over cold cases. by HAROLD J. BURSZTAJN

View Masters.....24

The remarkable triumphs of masters in the artist's studio—and even one in the batter's box—have realigned perceptions of vision. by MARGARET S. LIVINGSTONE AND BEVIL R. CONWAY

Bewitched, Bothered, and Bewildered.....32

Harvard physicians delve into the past to diagnose a range of mysterious maladies.

The Curious Case of the Incurable Epicure.....38

The sudden, baffling death of the grand admiral of the Dutch fleet handed a premier physician a mystery—and medical immortality.

by ANTHONY S. PATTON

Mystery Theater.....44

For more than a century, Harvard physicians have stepped into the clinical sleuthing arena to test their wits against some of medicine's most perplexing cases. by BEVERLY BALLARO

Name That Tool.....50

This quiz on antique medical instruments from the Warren Anatomical Museum may leave you aghast at the past. by VIRGINIA HUNT

Cover photograph of Alexander Calder taken in 1957 by Arnold Newman (courtesy of Getty Images).

In This Issue

PHYSICIANS SPEAK OF THEMSELVES AS "TAKING A HISTORY," BUT "TAKING a mystery" might well be the better term. Patients are often misled by the belief that their doctor will want a proper chronicle—only to be brought up short when the doctor says something like, "Just the facts, ma'am." When modern medicine tells a story, the genre it follows most closely is the mystery novel.

As a genre, mystery deals with a disruption in the order of things. In this it resembles comedy and tragedy, both of which begin with a loss—of order, propriety, property, or life—and end with an acceptance of that loss and with the restoration of order. In comedy the outcome is often a wedding; in tragedy it is a death. Because comedy reaches resolution through misdirection, humiliation, and rueful recognition, we in medicine try to avoid it, although we may join in the general delight of learning that the baby didn't *really* swallow the AAA battery, here it is after all under the couch, and weren't we all silly to have worried so much?

Whether a narrative of loss is a tragedy or a mystery depends largely on your point of view. In tragedy, the emotions of pity, fear, and catharsis arise from the fact that our proxy in the spotlight has tried and failed to do the right thing and now must suffer the consequences, extreme as they may be.

Mystery takes the elements of tragedy and moves them around. The characters that have created the story—victim and villain—are reduced to the stature of walk ons. The character of the chorus (renamed the "detective" ever since the appearance of some notable literary sleuths more than a century ago) is now the dominant one. Observation, inquiry, and moralizing no longer frame the story; they *are* the story. The tone is ultimately not passionate but intellectual. (Detectives with a personal stake in the outcome generally make for bad fiction, just as physicians with a personal stake may practice bad medicine.) The resolution of a mystery is not complete catharsis so much as simple relief that the puzzle has been solved and the pieces returned to their proper places.

Doctors as detectives, medicine as mystery—this issue of the *Bulletin* finds examples in the death of Julius Caesar (previously the subject of tragedy), the great tradition of the Cabot Cases at Massachusetts General Hospital, and the eyesight of Marc Chagall. The game is afoot...

William Ira Bennett

EDITOR-IN-CHIEF
William Ira Bennett '68

EDITOR
Paula Brewer Byron
ASSOCIATE EDITOR
Beverly Ballaro, PhD
ASSISTANT EDITOR
Janice O'Leary

BOOK REVIEW EDITOR
Elissa Ely '88

EDITORIAL BOARD
JudyAnn Bigby '78
Rafael Campo '92
Elissa Ely '88
Timothy G. Ferris '92
Alice Flaherty '94
Atul Gawande '94
Robert M. Goldwyn '56
Perri Klass '86
Victoria McEvoy '75
James J. O'Connell '82
Nancy E. Oriol '79
Anthony S. Patton '58
Mitchell T. Rabkin '55
Eleanor Shore '55

DESIGN DIRECTOR
Laura McFadden

ASSOCIATION OFFICERS
Joseph K. Hurd, Jr. '64, president
Steven A. Schroeder '64, president-elect 1
A. W. Karchmer '64, president-elect 2
Susan M. Okie '78, vice president
Phyllis I. Gardner '76, secretary
Kathleen E. Toomey '78, treasurer

COUNCILLORS
Nancy C. Andrews '87
Wesley A. Curry '76
Timothy G. Ferris '92
Gerald S. Foster '51
Donnella S. Green '99
Linda S. Hotchkiss '78
Lisa I. Iezzoni '84
Katherine A. Keeley '94
Kenneth I. Shine '61

DIRECTOR OF ALUMNI RELATIONS
Daniel D. Federman '53

ASSISTANT DIRECTOR OF
ALUMNI RELATIONS
Patrick Rivera

REPRESENTATIVES TO THE
HARVARD ALUMNI ASSOCIATION
Harold J. Bursztajn '76
Joseph K. Hurd, Jr. '64

The *Harvard Medical Alumni Bulletin* is published quarterly at 25 Shattuck Street, Boston, MA 02115 © by the Harvard Medical Alumni Association.
Phone: (617) 384-8900 • Fax: (617) 384-8901
Email: bulletin@hms.harvard.edu
Third class postage paid at Boston, Massachusetts. Postmaster, send form 3579 to 25 Shattuck Street, Boston, MA 02115
ISSN 0191-7757 • Printed in the U.S.A.

POW!

GROWING PAINS

I enjoyed reading "The Etiology and Treatment of Childhood," Jordan Smoller's excellent review paper on the Childhood Syndrome (Autumn 2004 issue of the *Bulletin*). I would like to add that recent evidence suggests that the Childhood Syndrome tends to progress inexorably to the Adolescence Syndrome, which has proven to be an infinitely more perplexing condition.

MASSAD GREGORY JOSEPH '77
SOUTH PASADENA, CALIFORNIA



Hazards of the Trade

Thank you for the literally hundreds of reminiscences that Pieter Kark '65 roused in the autumn issue about the Harvard Medical Services, which were once part of the Boston City Hospital. I graduated in 1947 and because of our "extended" fourth year, I spent five months there before starting my internship and assistant residency on the Second Medical Service, then a year at the Thorndike Memorial Laboratory.

In my day, Ward 2 was in a separate building. The experience was indeed unique. Most of the patients were indigent; many were alcoholics, usually with active delirium tremens requiring that we chase away the elephants and other threatening hallucinations. I learned much about protecting my valuables from two patients who were convicted burglars.

In addition to those in the Thorndike whom Dr. Kark mentioned, we were privileged to know Maxwell Finland '26; Henry Jackson, Jr.; Laurence Ellis '26; and

many others who, like William Castle '21 and Charles Davidson, became warm friends and mentors as well as wonderful teachers. And, finally, many of us rotated through the South Department, which was isolated across Mass. Avenue and housed contagious disease patients. I spent much of that rotation recovering from chicken pox!

I could go on and on, but I hope this letter will help to resurrect wonderful memories for those as lucky as I was to be a part of HMS at "The City."

GARTH K. GRAHAM '47
WEST CHESTER, PENNSYLVANIA

Naming Names

While perusing the reminiscence by Pieter Kark '65 about the Boston City Hospital in the Autumn 2004 issue of the *Bulletin*, I was stunned to see my photograph on page 43. As a research fellow in Charlie Davidson's laboratory, I studied liver disease and nutrition from 1955 to 1957. The smaller photograph, taken

in late 1956 or early 1957, depicts Leonore DeCarli, a remarkably able lab technologist, and me gazing at a Warburg respirometer. We were incubating thiamine deficient erythrocytes in the presence of methylene blue, which provoked a thiamine-dependent oxidative process. The larger photograph was taken on the same day, I believe, in the metabolic ward of the Thorndike Memorial Laboratory. The man in the foreground is Bernard Fast, a research fellow from Canada.

Those two years were wonderfully exciting and productive, and Charlie Davidson was indeed a superb mentor. But those years also made me realize the laboratory was not my métier.

STANLEY J. WOLFE '49
SAN FRANCISCO, CALIFORNIA

Joker's Wiles

I was greatly enthused by the humor issue but heartbroken at being left out of it, having been the coauthor, with Jimmy Kahn '67, of our class's Second and Fourth Year shows (and also having been librettist/lyricist/composer for my high school, internship, and residency shows).

Medical humor often comes from a slight extension of real medicine into the absurd. Please permit sharing of a belated bit: "Trouble in the neonatal ward: one of the newborns went into post-circumcision gonad storm; now two preemies have traumatic hymenotomies and one nurse is pregnant. (My God! What do we do?) Easy. Give the kid a shot of testicular antibodies, leading to Hashimoto's orchitis; end of problem."

A great issue, in any case.

THOMAS G. GUTHEIL '67
BROOKLINE, MASSACHUSETTS

The Bulletin welcomes letters to the editor. Please send letters by mail (Harvard Medical Alumni Bulletin, 25 Shattuck Street, Boston, Massachusetts 02115); fax (617 384 8901); or email (bulletin@hms.harvard.edu). Letters may be edited for length or clarity.



WICKED PITCH TO THE BEST: In this year's Second Year Show, four HMS students must escape a villainous pharmaceutical rep's scheme to ensnare them in a world of greed.

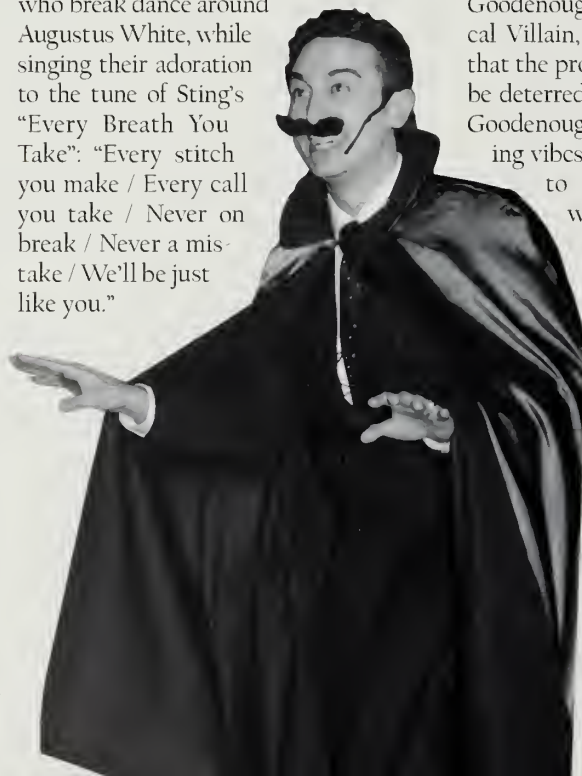
The Incredible Journey

IN THIS YEAR'S SECOND YEAR SHOW, "Into the Longwoods," four students negotiate the perils of an upside-down world created by a villainous pharmaceutical representative. The four students become trapped in an alternative reality after innocently accepting a free meal from a mustachioed, purple-caped scoundrel. In the course of their struggle to foil the villain's plot to transform them into his "prescribing machines," the students sing, dance, and satirize their HMS professors.

While stuck in the pharmaceutically funded neverland, the students receive dubious help from a Cheshire Cat ("Mad people, Med people—they seem the same to me"), a wolf suffering from a bad case of halitosis; step-dancing zombies; and a financial aid Pinocchio whose nose steadily lengthens as he enthusiastically pitches the advantages of student loans. In the end, it is a wizard—the incorruptible Dan Goodenough—who helps the stranded students find their way home.

But before they make it back to the Quad, the students must contend with

the Pharmaceutical Villain's dastardly scheme to separate them from one another. The fiendish drug rep concocts one temptation after another to try to keep them in his clutches. The first student to abandon the group is Wayne, mesmerized by a troupe of surgical students who break dance around Augustus White, while singing their adoration to the tune of Sting's "Every Breath You Take": "Every stitch you make / Every call you take / Never on break / Never a mistake / We'll be just like you."



The next to succumb is Carla, who runs off with Robin Hood (James O'Connell '82, director of Boston's Health Care for the Homeless) and his Merry Men. But she then abandons him to join the entourage of female admirers surrounding Paul Farmer '90 in the cloud kingdom he inhabits. Farmer's fans swoon as he and Carla warble a duet set to the tune of "A Whole New World" from Disney's *Aladdin*: "A new third world! / Infectious microbes to destroy / Malaria, AIDS, TB / I guarantee / will end because of me. / A new third world! / I am the key / We'll reach new heights / of human rights / because of me."

Next Grace is lured to an enchanted castle, where an "Academic Beast"—Rick Mitchell '84—toils away with his graduate students forever cursed to a life of academic medicine. The students, some of whom have taken to dressing as lab equipment, have forgotten the outside world. Their ranks include Binary Guy, who speaks exclusively in ones and zeroes.

Only Frank is left to reunite the group. With the aid of a Tooth Fairy Godmother, Frank throws a bash attended by all the Longwoods inhabitants. There Dan Goodenough confronts the Pharmaceutical Villain, who is stunned to discover that the professor is simply "too chill" to be deterred by the Valium flung at him. Goodenough melts the villain with loving vibes and sends the students back to the Quad with some final words of wisdom: there's no such thing as a free lunch.

"Putting together the show was a true bonding experience for our class," says director Alyssa Rosen '07. "I felt inspired by my classmates' diverse talents and the tremendous support we received from each other and from the faculty, especially those we lampooned." ■

Resident Export

THE 53RD ANNUAL MATCH DAY, HELD March 17, revealed to 156 HMS fourth-year students where they will be spending their residencies. Half of the students will remain in Massachusetts, with almost all of them (96 percent) working for HMS programs. Of the rest, 22 percent will head to California and 11 percent to New York. Internal medicine was the most popular specialty, attracting almost a third of the class. Pediatrics, with 11 percent, was the second most popular, closely followed by emergency medicine, chosen by 10 percent. Compared to last year's class, dermatology, psychiatry, and radiology saw a decrease while family practice, orthopedics, and general surgery saw an increase.



ANESTHESIOLOGY

Walter Bethune

Massachusetts General Hospital

Christopher Connor

Brigham and Women's Hospital

Christina Fidkowski

Massachusetts General Hospital

DERMATOLOGY

Deborah Goddard

University of California—San Francisco

Brian Somoano

Stanford University Programs

Hien Tran

New York University School of Medicine

Thanh-Nga Tran

Massachusetts General Hospital

Sarvenaz Zand

University of California—Davis Medical Center, Sacramento

EMERGENCY MEDICINE

Olabolanle Ayodele

Brigham and Women's Hospital

Jamil Bitar

University of Arizona Affiliated Hospitals

Uche Blackstock

SUNY Health Science Center, Brooklyn

Eduardo Borquez

University of Southern California, Los Angeles

Robert Casey

UCLA Medical Center

Alison Lozner

Brigham and Women's Hospital

Robert Mittendorf

Stanford University Programs

Sara Nelson

Brigham and Women's Hospital

Lauren Nentwich

Boston University Medical Center

Uta Shimizu

Harbor—UCLA Medical Center, Torrance, California

Kurt Smith

University Hospital of Cincinnati

Kavid Udompanyanan

UCLA Medical Center

Benjamin White

Brigham and Women's Hospital

Dayle Whiteman

University of Chicago Hospital

FAMILY MEDICINE

Frances Baxley

University of California—San Francisco

Catherine Livingston

Oregon Health and Science, Portland

Erin Lunde

Sutter Medical Center, Santa Rosa, California

Christiana Nwofor

Jamaica Hospital Medical Center, Jamaica, New York

GENERAL SURGERY

Dawn Barclay

Dartmouth—Hitchcock Medical Center

Loretta Erhunmwunsee

Duke University Medical Center

Gregory Feldman

Stanford University Programs

Joan Hu

Massachusetts General Hospital

Alexander Iribarne

New York Presbyterian Hospital—Columbia

Eric Jelin

University of California—San Francisco

Eric Sheu

Brigham and Women's Hospital

Elisabeth Tomlinson

Duke University Medical Center

INTERNAL MEDICINE

Hans Ackerman

Massachusetts General Hospital

Francis Alenghat

Brigham and Women's Hospital

MaryCatherine Arbour

Brigham and Women's Hospital

Rebecca Berman

Brigham and Women's Hospital

Oni Blackstock

Einstein/Montefiore Medical Center, New York

Rebecca Brown

University of California—San Francisco

Anh Bui

University of California—San Francisco

Linda Calvillo

University of Texas Southwest Medical School, Dallas

Bradley Carthon

Massachusetts General Hospital

Alejandra Casillas

University of California—San Francisco

Megan Coffee

Massachusetts General Hospital

Eric Dean

University of California—San Francisco

Sherry Farzan-Kashani

New York Presbyterian Hospital—Cornell

Jeremy Greene

Brigham and Women's Hospital

Reena Gupta

New York Presbyterian Hospital—Columbia

Prasanna Jagannathan

University of California—
San Francisco

Simonette Jones

Tulane University School of
Medicine, New Orleans

Jared Kesselheim

Massachusetts General Hospital

Kumaran Kolandaivelu

Brigham and Women's Hospital

Daniel Kramer

Massachusetts General Hospital

Evan Lau

Massachusetts General Hospital

Michele Lee

Stanford University Programs

Kedar Maté

Brigham and Women's Hospital

Jacinda Mawson

Brigham and Women's Hospital

Margaret McNairy

Brigham and Women's Hospital

Alanna Morris

Brigham and Women's Hospital

Gabriela Motyckova

Massachusetts General Hospital

Connie Ng

Massachusetts General Hospital

Enyi Nwaneri

Johns Hopkins Hospital

Gabrielle Page-Wilson

Brigham and Women's Hospital

Channing Paller

Johns Hopkins Hospital

Maria Said

Johns Hopkins Bayview
Medical Center

Paul Sepe

Massachusetts General Hospital

Parmanand Singh

New York Presbyterian
Hospital—Cornell

Laura Tarter

Brigham and Women's Hospital

Lauren Thronson

University of Washington
Affiliated Hospitals

Anand Vaidya

Brigham and Women's Hospital

Jesus Vazquez

Brigham and Women's Hospital

Vladimir Vinarsky

New York Presbyterian
Hospital—Columbia

Nikhil Wagle

Brigham and Women's Hospital

Susan Zhao

Massachusetts General Hospital

Hao Zhu

University of California—
San Francisco

INTERNAL MEDICINE/ PEDIATRICS

Natalie Dailey

Baylor College of Medicine,
Houston

Paritosh Prasad

Massachusetts General Hospital

Joel Sawady

Massachusetts General Hospital

NEUROLOGY

Heather Gunter

University of Pennsylvania,
Philadelphia

Amy Lee

University of California—
San Francisco

Joshua Shulman

HMS/Massachusetts General
Hospital/Brigham and Women's
Hospital

NEUROSURGERY

Eric Chang

Harvard/Massachusetts
General Hospital

Carlos Ledezma

University of Southern Califor-
nia/Los Angeles City Hospital

Nestor Tomycz

University of Pittsburgh

OB/GYN

Ann Chang

University of Hawaii, Honolulu

Angie Child

University of California—
San Francisco

Joshua Klein

Brigham and Women's
Hospital

Sierra Washington

University of California—
San Francisco

OPHTHALMOLOGY

Yassine Daoud

Duke University Medical Center

Shelley Day

University of California—
San Francisco

Shaheen Karim

UCLA/Jules Stein Eye Institute
EyeSTAR Program

Shana McCormack

University of California—
San Francisco

Charles Wykoff

University of Miami/Bascom
Palmer Eye Institute

ORAL AND MAXILLOFACIAL SURGERY

Nancy McDermott

Massachusetts General Hospital

Daniel Richardson

Massachusetts General Hospital

Christian Rouleau

Massachusetts General Hospital

ORTHOPEDIC SURGERY

Christina Boulton

Massachusetts General Hospital

Grant Garrigues

Duke University Medical Center

Albert Lin

Massachusetts General Hospital

Andrew Malin

University of Iowa Hospitals and
Clinics, Iowa City

Manish Sethi

Massachusetts General Hospital

OTOLARYNGOLOGY

David Rosow

Columbia University

Aaron Wieland

HMS/Massachusetts Eye and Ear
Infirmary

PATHOLOGY

Scott Boyd

Stanford University Programs

PEDIATRICS

Elizabeth Baca

University of California—
San Francisco

Margret Bock

McGaw Medical Center of
Northwestern University/
Children's Memorial Hospital

Joshua Borus

New England Medical Center



PHOTOS: IZAA-CARTEN



Samira Brown

Children's Hospital, Boston

Laura De Girolami

Massachusetts General Hospital

Hannah Galvin

McGaw Medical Center of
Northwestern University/
Children's Memorial Hospital

Colleen Hanna-Slagle

Baylor College of Medicine
Houston

Anne Light

Massachusetts General Hospital

Azure Makadzange

Children's Hospital, Boston

Lisa McLeod

Massachusetts General Hospital

Deborah Mitchell

Massachusetts General Hospital

Ann Ramsey

University of Washington
Affiliated Hospitals

Annemarie Stroustrup Smith

Mount Sinai Hospital, New York

Ari Wassner

Children's Hospital, Boston

Michael Williams

Medical Center of Central
Georgia, Macon

Bergen Nelson

University of California-
San Francisco

PHYSICAL MEDICINE/ REHABILITATION

Michael Turner

Mayo Graduate School of
Medicine

PLASTIC SURGERY

Marco Ellis

McGaw Medical Center of
Northwestern University

Allen Liu

Brigham and Women's Hospital

Wojciech Przylecki

Brigham and Women's Hospital

PSYCHIATRY

Margot Albeck

Massachusetts General
Hospital/McLean Hospital

Ariadna Forray

Yale-New Haven Hospital

Cassie Henry

University of California-
San Francisco

Karimi Mailutha

New York Presbyterian
Hospital-Columbia

Alison May

University of California-
San Francisco

Sarah Russell

New York Presbyterian
Hospital-Columbia

RADIATION ONCOLOGY

Andrew Elia

Brigham and Women's Hospital/
Massachusetts General Hospital

Paiman Ghafoori

Duke University Medical Center

Larissa Lee

Brigham and Women's Hospital/
Massachusetts General Hospital

Abraham Wu

Memorial Sloan-Kettering
Hospital, New York

RADIOLOGY

Lauren Carter

Hospital of the University of Penn-
sylvania Philadelphia

Lawrence Cheung

Stanford University Programs

Gabriel Gonzalez

Santa Clara Valley Medical
Center, San Jose

Kevin King

University of Texas Southwestern
Medical School Dallas

Jonathan Murnick

Massachusetts General Hospital

Tamara Oei

Brigham and Women's Hospital

UROLOGY

Audley Osbourne

Massachusetts General Hospital

OTHER

Martin Burke

Assistant Professor of Chemistry,
University of Illinois, Urbana

Joseph Corkery

OpenEye Scientific Software,
Cambridge, Massachusetts

Anita Goel

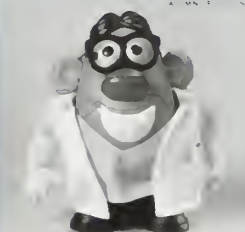
Research

Arif Nathoo

Associate Consultant, McKinsey
and Company, Florham Park,
New Jersey

WINNING WAYS

Harvard Medical



This Spud's for You

The *Bulletin* recently won a gold medal from the Council for Advancement and Support of Education (CASE) in the professional and graduate school magazine category based on its Spring 2004 and Autumn 2004 issues. CASE also awarded the *Bulletin* a silver medal in the periodical special issues category for its special report on humor in medicine, which featured Dr. Potato Head on its cover.

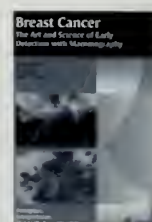
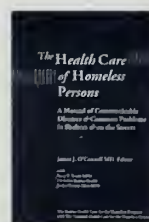
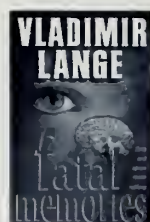
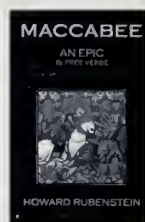
Sixteen Candles

In its annual roundup of the country's best graduate schools, *U.S. News & World Report* has named HMS the best medical school in the research category for the 16th year in a row, with an overall perfect score. The remaining top five medical schools, in order, are Johns Hopkins University; Washington University in St. Louis; the University of Pennsylvania; and the University of California, San Francisco.

PEDIATRICS/ PRIMARY CARE

Jamal Harris

Einstein/Montefiore Medical
Center



Maccabee

An Epic in Free Verse, by Howard Rubenstein '57 (Granite Hills Press, 2004)

In this fictional interpretation of four books of the biblical Apocrypha, Rubenstein, a retired internist, tells the story of the first recorded battle for religious freedom. For 30 years, Judah Maccabee—"the hammer"—and his warrior brothers railed against the Greek tyrants and soldiers who occupied Judea during the second century B.C.E. The Maccabees' eventual triumph led to the first celebration of Hanukkah.

Understanding Paranoia

A Guide for Professionals, Families, and Sufferers, by Martin Kantor '58 (Praeger Publishers, 2004)

Kantor, a psychiatrist, presents the characteristics, causes, and treatments of paranoia. He offers advice for contending with paranoid people at home or at work, cautions professionals to use affirmative approaches, and discusses the promise and pitfalls of pharmacotherapy. The final chapter directly addresses paranoid men and women and offers sympathetic strategies for coping with the disorder.

Occupational Musculoskeletal Disorders

by Nordin M. Hadler '68 (Third edition, Lippincott Williams & Wilkins, 2005)

Hadler, an internist and rheumatologist who specializes in occupational medi-

cine, details the most widespread, job-related musculoskeletal and neurovascular disorders, focusing on the knee, hip, foot, hand, arm, and shoulder. He devotes several chapters to issues of disability and worker's compensation and includes a discussion of ergonomics.

Fatal Memories

by Vladimir Lange '72 (Red Square Press, 2005)

In this medical thriller, an HMS-educated neuropsychiatrist haunted by a recurring nightmare throws herself into the clinical trials for her invention—a device that can target and erase traumatic memories. She travels to Moscow, where her project, sanity, and life become threatened by a 600-year-old chain of events. Lange, a former emergency room physician, has a talent for plot twists that make this story crackle with surprises.

The Health Care of Homeless Persons

A Manual of Communicable Diseases & Common Problems in Shelters & on the Streets, edited by James J. O'Connell '82, with Stacy E. Swain, Christine Loeber Daniels, and Joslyn Strupp Allen (Boston Health Care for the Homeless Program, 2004)

The diagnoses clinicians are likely to see in shelters range from bed bugs to frostbite to hepatitis. O'Connell includes the prevalence, transmission, symptoms, and treatments for each problem. Full color photos complement each chapter,

and charts detail the costs of various medications. Fact sheets in English and Spanish have been included to educate patients about the most prevalent infectious diseases.

The Optimist

Meditations on Medicine, by Howard M. Spiro '47 (Science & Medicine, 2004)

This volume collects 45 of Spiro's eloquent musings from his column in *Science & Medicine* on patients, science, human nature, and even the vagaries of medical language. For example, he writes that he prefers "patients" over "clients" and approves replacing "abdomen" with "belly." He combines a warm, mentoring tone with flashes of humor in this call for a deeper engagement in patients' lives.

Breast Cancer

The Art and Science of Early Detection with Mammography, by László Tabár, Tibor Tot, and Peter B. Dean '70 (Thieme, 2005)

This text reaffirms the importance of early detection in treating breast cancer and guides physicians in making correct diagnoses. It presents detailed and illustrated instructions for determining parenchymal patterns to help differentiate between healthy and abnormal tissue. The authors pay special attention to cooperation between pathologists and radiologists, provide a systematic method for evaluating mammograms, and review the merits of several techniques.

Seascapes

by David Sanders Howell (*Howell, 2004*)

A COUSIN OF MINE WAS A COLERIDGE SCHOLAR AT A HIGH-MINDED and costly university. Students flew from all over the country to study with him. An excellent teacher, he inspired many undergraduates to undertake a lifetime of scholarship. But all along, it turns out, he didn't want to be a professor. He wanted to be an art critic. An abstract art critic. So, in his sixties, he became one.

True Renaissance mastery is impossible. We cannot be everything we want to be; it's like trying to climb all the Himalayas, when a single mountain is a life accomplishment. Most of us summit only once professionally, and even then—as in medicine—peaks upon peaks of subspecialization emerge. The flag takes a long time to plant. Then, years later, one quietly remembers what else one yearned to do.

So the emergency room doctor pulls out an old African drum and takes lessons. The cardiologist joins a church choir. Far too many psychiatrists write. And then there are artists.

David Sanders Howell '47 has been a professor of medicine at the University of Miami since 1967. He founded its arthritis division and has written hundreds of textbook chapters and manuscripts. In the spare introduction to his self-published book of oil paintings, *Seascapes*, he recalls being "stirred" as an 11-year-old boy by an ocean painting in his local museum. But art lessons gave way to chemistry lessons, and eventually, successfully, to medical school. The long vertical ascent had begun.

In the 1970s, while at the top of his Everest in Miami, where he was established as an international expert in the mineralization of cartilage, Howell returned to painting. He painted in England and Italy, Maine and California, Key Largo and Gloucester—apparently anyplace oceanic. He writes, in *Seascapes*, "When I am asked what other subjects I enjoy painting besides the ocean, my reply is that I have never tired of addressing the majestic sea."

Howell probably didn't publish his book for review. His painting is no doubt a quest for respite, not scrutiny. But here comes a confession: it turns out we all want to be art critics. Presented with the opportunity, which may never arise again, I cannot pass up the temptation.

Given the chance, my cousin would pause in front of each plate in *Seascapes* for a long time. He would notice this technique, that shadow, these deliberate lines and intentional colors. He would be hard at work noticing. I know this because I've gone to museums with him, and we'd still be standing in front of a painting long after I would have preferred to be sitting in front of lunch.

But I'm a different kind of art critic, and this is a different kind of review. There will be nothing about Howell's school of technique or use of color; no cogent words on his brush strokes. There is not even an eye for particulars—though I can report plenty of traditional seafare: sunrises and sunsets, bracing winds tipping sails in all directions, tides, docks, fogs, moonlight, reflections, high and low clouds of every color, and one seagull cruising leisurely toward eternity. People don't matter much in these paintings, which is interesting, since people are all that matter in medicine.

What does matter in these paintings is their affecting representation of passion. A man at the pinnacle of his career paused to watch the ocean move, again and again, in every corner of the world. Taken together, the book is a portrait of a life outside the joints and cartilages that made the painter

famous. These are the views that captivated and sustained him.

Though all are evocative, my favorite image in *Seascapes* is actually not a painting at all. It is a photograph. Against pale yellow light, Howell sits in profile on a stool, sketching a tidal flat. He's wearing a windbreaker. His socks are covered with sand. His mouth is slightly open, as if he is dumbfounded by what he sees. One hand holds a pencil, poised over its pad. I love this photo, because it's the portrait of a man on his mountaintop. ■

Elissa Ely '88 is a psychiatrist at the Massachusetts Mental Health Center and the Boston Health Care for the Homeless Program.



OIL AND WATER: David Sanders Howell has spent decades translating his visions of the sea onto canvas.



PRESIDENT'S REPORT

Many Happy Returns

THE SEARCH FOR THE SUCCESSOR TO DANIEL FEDERMAN '53 as director of alumni relations recently concluded with the appointment of George Thibault '69. Many alumni know George as a practicing physician in the Partner's HealthCare System and as the director of the Academy at the School. He was also recently honored with the Daniel D. Federman Professorship in Medicine and Medical Education at HMS. We feel confident that he will extend the tradition of excellence demonstrated by his predecessors and look forward to welcoming him at the next Alumni Council meeting.

George will work closely with the alumni office, which has adjusted well to its reduced work force, the result of the budgetary restrictions mentioned in my last report, and Dan Federman, I am pleased to note, will continue to interact with alumni in his new part-time role working with the Office of Resource Development. Dan has an ongoing interest in developing a program to promote lifelong learning for alumni, using the rich resources of our faculty, the continuing medical education offerings, and the print and electronic media. We're grateful to Dan for letting us down gently, by retiring in stages. He has been a memorable force at the School for five decades.

Along with Harold Bursztajn '76, I serve as a liaison from HMS to the Harvard Alumni Association. At our most recent meeting, we heard a progress report on the initiative President Larry Summers proposed almost two years ago to create a Common Alumni Affairs and Development Office (CAAD). This involved creation of a university-wide database, with one computer system for recording registration data, participation in alumni activities, and giving history. This program, using a third party vendor, has now started at two graduate schools and will be coming to HMS in the fall. It will eventually permit

all the graduate school alumni offices at Harvard to share best practices and successful programs, avoiding unnecessary and expensive duplication of efforts.

The university will also be participating in a new affinity credit card program through Barclays Bank, with benefits and rewards specifically tailored to Harvard. The MasterCard, to be available in July, will offer a favorable maximum APR (perhaps 7.9 percent), a 60-day grace period, and no annual, ATM, or foreign exchange fees. In addition to standard "points" for business use, holders can secure double points by choosing to pay Harvard dues, reunion fees, and similar expenses with this card.

The income derived from the arrangement with Barclays will go exclusively to the Presidential Scholars program, which Larry Summers created in 2002. Initially funded at \$14 million, this program brings people interested in furthering their careers in public service or research to Harvard for a year of scholarship at the master's or doctoral level. The first class of scholars included two physicians. One, a pediatrician from the former Soviet Republic of Georgia who has been active at the World Bank,

now seeks additional training to exert a larger influence on economic policy in Georgia. The other, an obstetrician-gynecologist who was forced out from Afghanistan by the Taliban, is studying at the Harvard School of Public Health with the hope of returning to play a larger role in public health as that country's director of UNICEF.

We expect these new university-wide programs to affect the work of the alumni office and the Council over the next few years. ■

Joseph K. Hurd, Jr., '64 is chairman emeritus of the Department of Gynecology at the Lahey Clinic Medical Center in Burlington, Massachusetts.



STAGED EXIT: Daniel Federman has retired as director of alumni relations but will continue to serve Harvard Medical School in a part-time role.



Science Friction

BEST-SELLING AUTHOR MICHAEL CRICHTON '69 RECENTLY published a novel, *State of Fear*, in which a brilliant MIT professor and a beautiful lawyer uncover a plot by environmental terrorists who have unleashed a series of catastrophic, seemingly natural events to call attention to the dangers of global warming. Woven into this story are unscrupulous scientists who doctor data to obtain more money and assorted well-meaning, impressionable people who start out believing that the threat of global warming is real, but who eventually see the light when confronted by the professor's compelling arguments. Were it left at that, *State of Fear* would be just another thriller.

But instead Crichton, under the guise of a novel, presents a broad-based attack on the environmental movement, complete with graphs and references. From a scientific perspective, the book is deeply flawed. For one, Crichton ignores most of the peer-reviewed literature on climate change, and many of his statements lack substantiation. His logic also is faulty. He writes in an appendix, for example, that just as prominent scientists

Third, and most important, is the issue of what's at stake. During medical school, we learned that if evidence of great harm to a patient was compelling enough, we had to intervene, even before all the tests were in. The classic example of this "precautionary principle," so fundamental to clinical medicine, is appendicitis, where, despite a convincing history and supporting physical exam, lab tests, and x-rays, it's sometimes still impossible to say with certainty that the patient has appendicitis. Surgeons must operate. They can't afford to wait for absolute proof, for doing so might mean a ruptured appendix, peritonitis, and fatal septicemia. They can't risk being wrong.

Such is also the case with global warming, but here we're dealing with the lives of billions of people. The evidence is overwhelming that the carbon dioxide we're releasing in ever-increasing amounts into the atmosphere, where it lasts more than a hundred years, is the main reason that global temperatures are climbing, ice sheets are melting, sea levels are rising, extreme weather events such as heat waves are increasing in number and intensity, ecosystems are threatened, and patterns of infectious



Michael Crichton's assessment that we know "astonishingly little" about the global environment should make him humbler and far more cautious.

of the early twentieth century advocated eugenics, a notion later discounted, the science of global climate change, supported by leading scientists of our time, will end up discredited as well.

It is hard to take Crichton's anti-environmental arguments seriously. But, as he is a Hollywood icon whose Harvard degrees give him credibility, and as his viewpoints are increasingly quoted by those seeking to attack the legitimacy of climate change science—such as James Inhofe, a Republican senator from Oklahoma who has called global warming "the greatest hoax ever perpetrated on mankind"—take him seriously we must.

I will limit myself to three points about Crichton and his book. First, he seems to contend that those who express alarm about the consequences of environmental degradation are driven primarily by power and greed, rather than by a deep concern for life on this small planet. Given how politically powerful environmental groups seem to be these days, especially about global warming, and the pathetic under-funding of environmental research, such a claim is laughable.

Second, though Crichton has no background in the field, he seems convinced that after three years of study, he understands global climate change in ways that have somehow eluded thousands of the world's top experts.

diseases are changing. If we don't take these observed events seriously and act now to lessen their growing impact, if we wait until we have 100-percent proof of where they're heading, we may be too late to avoid public health catastrophes in coming decades.

Crichton's assessment that we know "astonishingly little" about the global environment should make him humbler and far more cautious. Shouldn't we be doing everything possible to avoid disrupting the planet's physical, chemical, and biological systems on which all life depends, especially when we don't fully understand them? If we're guessing, as Crichton and some in Washington seem to be doing, that the dangers of altering these systems are minimal, can we risk being wrong?

Great celebrity carries with it great responsibility. Michael Crichton had the opportunity to reach large numbers of people with a careful evaluation of the science of global warming and to educate them about its enormous potential dangers. Instead, his book is misleading and irresponsible, and it would be a tragedy if it were considered to be anything other than fiction. ■

Eric Chivian '68, director of the Center for Health and the Global Environment at Harvard Medical School, shared the 1985 Nobel Peace Prize as co-founder of International Physicians for the Prevention of Nuclear War.

Of Mice and Men

RESearchers at Harvard Medical School and its affiliated institutions continue to demonstrate why *U.S. News & World Report* has ranked HMS first among medical schools every year since the list began. A few of the School's many recent findings:

Statin Feats

Researchers at Children's Hospital Boston have shown that high blood cholesterol levels accelerate prostate cancer at the molecular level. By altering chemical signaling patterns within tumor cells, cholesterol helps the tumors to survive and grow. The findings, which appear in the April 1 issue of the *Journal of Clinical Investigation*, are in keeping with population studies that have linked prostate cancer with high cholesterol levels and rich Western diets. Led by Michael Freeman, the researchers also present evidence that cholesterol-lowering statin drugs, now widely used to combat cardiovascular disease, may inhibit cancer growth.

Night Vision Boggles

Scientists at the Massachusetts Eye and Ear Infirmary have discovered a mutation in a gene that interferes with electrical signaling in the retina and causes a newly recognized form of abnormal vision associated with night blindness. Their findings appear in the March 29 issue of the *Proceedings of the National Academy of Sciences*. According to lead author Thaddeus Dryja, the newly recognized defect provides scientists with fresh insights into how the eye processes visual information.

Defensive Treasures

Angiogenesis inhibitors, which block blood vessel formation, have become a hot area of research for cancer treatment. A recent study led by Raghu Kalluri of Beth Israel Deaconess Medical Center suggests that natural angiogenesis inhibitors in the body actively work to keep tumors from growing. The findings, published in the February 22 issue of the *Proceedings*

of the National Academy of Sciences, show that in mice lacking these defensive molecules, tumors progress much more rapidly than they normally would. This line of research is bringing about a new approach to cancer treatment and prevention that focuses on boosting the body's natural defenses against cancer's spread.

Deficit Mending

Hemochromatosis, or iron overload disease, is one of the most common genetic diseases and among the most baffling. Tissues such as liver, pancreas, and heart become packed with iron. Yet macrophages, whose job it is to store and recycle the iron from aging red blood cells, exhibit unusually low levels of the mineral. Why does iron build up in the tissues and not in the normally iron-rich macrophages? Adriana Donovan, Nancy Andrews '84, and their colleagues at Children's Hospital Boston may have found an answer to the decades-old conundrum. It appears that the protein ferroportin is the only

THE EYES HAVE IT



ANYONE WHO HAS STUDIED A LANGUAGE AS AN ADULT HAS struggled to reshape the brain's connections. One key scientific window into how experience molds the brain is the development of the mammalian visual cortex, which must receive input from both eyes during a critical period to enable binocular vision. Carla Shatz, the Nathan Marsh Pusey Professor of Neurobiology at HMS, and colleagues devised a technique for following development in the visual cortex of mammals by looking at expression of the *arc* gene. Their results appear in the March issue of *Nature Neuroscience*.

Scientists believe the brain initially develops according to a fixed program and then enters a stage at which it is shaped by sensory experience of the environment. Once this stage ends, the brain becomes less malleable. In mice, for instance, if one eye is disabled during the critical period for plasticity in the visual cortex—between 25 and 35 days of age—neural

If the epidemic of child and adolescent obesity continues unabated, life expectancy in the United States could be shortened by two to five years in the coming decades.

mechanism mammalian cells have for exporting iron. And hemochromatosis may result from too much of this iron exporter. The findings, reported in the March issue of *Cell Metabolism*, suggest new approaches to treating the disease, which currently affects approximately one in 200 Caucasian Americans.

Built-In Pool

A study in mice reveals that the placenta serves as a temporary home for a large pool of blood-forming stem cells during fetal development. The research, led by Hanna Mikkola and Stuart Orkin '71 at Children's Hospital Boston and published in the March issue of *Developmental Cell*, solves a longstanding riddle about the origin of the cells that form the hematopoietic system. Stem cells require special environments that allow them to grow and divide without differentiating into specific cell types. Studying how the placenta nurtures these cells may point to ways of cultivating them for bone marrow transplantation and other uses.

What to Inspect When You're Expecting

Use of the anticonvulsant drug valproate during pregnancy may pose a significantly greater risk of birth defects than does use of other antiseizure medications. In the March 22 issue of *Neurology*, senior author Lewis Holmes, chief of the Genetics and Teratology Unit at the MassGeneral Hospital for Children, and colleagues report that women taking valproate alone faced a fourfold increased risk of giving birth to a child with a major malformation, compared with the risk among women taking other anticonvulsants. Sold in the United States under the brand names Depakote and Depakene, valproate is used to treat seizures, migraines, and such psychiatric illnesses as bipolar disorder.

Premature Girth

A broad assumption has been that U.S. life expectancy would continue to increase indefinitely. But a new data analysis, published in the March 17 issue of *The New England Journal of Medicine*,

PHOTO: JAY MCINNIS/TAXI



suggests that this trend is about to reverse itself because of the rapid rise in obesity, especially among children. A review by David Ludwig of Children's Hospital Boston, S. Jay Olshansky of the University of Illinois at Chicago, and colleagues concludes, according to a conservative estimate, that obesity now reduces the average U.S. life expectancy by four to nine months. The researchers also predict that, if the epidemic of child and adolescent obesity continues unabated, life expectancy could be shortened by two to five years in the coming decades. ■

connections rearrange to make the working eye dominant. Other species and other brain functions are shaped in similar ways, though the molecular machinery behind plasticity during the critical period is not known.

Researchers in Shatz's laboratory used the expression of the *orc* gene to identify neurons that become more or less active in response to visual experience or deprivation. (The function of *orc* is not clear, but approximately 30 minutes after a visual stimulus, its expression increases several orders of magnitude in neurons of the visual cortex receiving input from the stimulated eye.)

The *orc*-induction method yielded information about plasticity in three dimensions across the entire visual cortex of mice, leading to some surprising results. Arc induction revealed a critical period that began earlier and continued much later than expected. Previous techniques had only monitored the surface layers of the visual cortex or a small neuron responsible for binocular vision.

In the cat, a more visual species, the findings differed. "In the cat, there have been no surprises so far," says Patrick Konold, a co-first author of the paper and an instructor in neurobiology at HMS. "Our research confirmed 50 years of data." The investigators plan to use genetic techniques in mice to zero in on molecular mechanisms of plasticity during critical periods, then work back to more complex mammals, including humans.

"The work in the lab is directly related to childhood learning and disorders of development," says Shatz. "You can't address issues such as autism and dyslexia without a basic understanding of normal brain development." Now that the *orc* method has proved a useful complement to established techniques, she promises more molecular findings on plasticity in the future. ■

Toi Viinikko is a former intern of Focus.

The Kindest Cut of All

BY THE TIME SEIZURES OR OTHER symptoms have persuaded someone to seek medical care for a low-grade glioma, a few tumor cells have already infiltrated tissue beyond the visible white mass on the brain scan. Surgery falls short of a cure, but it is the cornerstone of treatment. Removing as much of a tumor as is safely possible will extend and improve the lives of afflicted people for years or even decades, doctors believe. Yet that plausible idea has turned out to be remarkably difficult to prove.

A new study of neurosurgery patients at Brigham and Women's Hospital (BWH) bolsters the case for aggressive surgery to excise low-grade gliomas, says Elizabeth Claus, an associate neurosurgeon at BWH. Claus and her colleagues followed the outcomes of 156 patients for an average of three years after surgery. People whose tumors could be only partially removed were 1.4 times more likely to relapse and 4.9 times more likely to die than people whose postoperative brain scans showed no traces of remaining tumor, the researchers report in the March 15 issue of *Cancer*.

"If we can safely take all the imaged tumor out, patients will be better off," says senior author Peter Black, chief of neurosurgery at BWH and Children's Hospital and the Franc D. Ingraham Professor of Neurosurgery at HMS. "The trick is knowing where the tumor is, exactly; knowing that taking it out won't hurt valuable brain tissue; and knowing when the tumor is gone."

To the naked eye, the tumors so closely resemble healthy brain tissue that even the most experienced neurosurgeons may have trouble confirming that they have removed all possible traces of the abnormal growth. Historically, many doctors and their patients have favored a watch-and-wait approach, postponing risky brain surgery until more serious symptoms develop, and then perhaps prescribing radiation as a first-line treatment.

More recently, studies have suggested people will live longer if more of their tumors are removed, but those studies are far from conclusive. Some retrospective analyses have shown that total removal of a low-grade glioma can delay or prevent it from growing into a malignant cancer and can extend life, but others have suggested that radiation therapy may make full resection less important.

Low-grade gliomas start in the glial cells that support and surround the neu-

rons. They usually grow slowly, but most of them eventually turn malignant. In fact, about one-third of Black's patients who appear to have a low-grade tumor have one that has begun to transform into a malignant cancer extending invisible arms into the brain. "Part of why this is so important," Claus says, "is that it affects young people in the prime of life."

Gliomas are less common than the number of people in the study might suggest. About six cases for every

"If we can safely take all the imaged tumor out, patients will be better off," says neurologist Peter Black. "The trick is knowing where the tumor is, exactly; knowing that taking it out won't hurt valuable brain tissue; and knowing when the tumor is gone."



A Heartbeat Away

100,000 people are diagnosed each year in the United States. But BWH has become a center for treating the low-grade tumors and draws a disproportionate number of people with a preliminary diagnosis and desire for surgery, Black says. The attraction is an operating suite that allows real-time imaging during surgery to confirm the presence or absence of residual tumor. To date, more than 700 people have undergone a craniotomy for biopsy or surgery in the BWH unit.

Studies by Black and others have shown that intraoperative MRI enables surgeons to remove a greater portion of the malignancy safely. According to Claus, the new study aimed to address the role of surgery with more statistical precision. "It is not known with certainty if surgical resection is the ultimate therapy for people with low-grade gliomas in terms of long-term survival," she says.

Ultimately, the study does not provide the long-sought authoritative answer to the question, says Henson. "I do think that intraoperative MRI is the wave of the future and that it leads to better resections," he adds. "It just is difficult to formally prove that better resections lead to better survival."

The current analysis falls short of definitive evidence, Claus agrees, because it is subject to the biases inherent in a retrospective, hospital-based study. "The next step is to examine this question within the setting of a clinical trial or population-based study," says Claus, who hopes to look at more data from other centers that treat low-grade gliomas. Further analyses will include data on genetic variants to elucidate the effect of such information on neurosurgical outcomes. ■

Carol Cruzan Morton is a science writer for Focus.

PLATELETS OFTEN CONTINUE TO stick together in the aftermath of a heart attack, causing arteries that were opened to close back down and triggering a second heart attack, a stroke, or even death. To improve recovery, clot-busting cocktails may soon include a new component, the antiplatelet agent clopidogrel, which was evaluated in a study in the March 24 issue of *The New England Journal of Medicine*. Lead author Marc Sobotine '94, an HMS instructor in medicine and a cardiologist at Brigham and Women's Hospital (BWH), says the drug is the first pharmacological advance in treating serious heart attacks in more than a decade.

Clopidogrel is already a proven treatment for some kinds of cardiovascular disease, including less severe heart attacks. Would adding it to the standard fibrinolytic regimen improve outcomes for the most acute myocardial infarctions? Senior author Eugene Braunwald, the Hersey Distinguished Professor of Theory and Practice of Physics at HMS and BWH, raised this question to the longstanding Thrombolysis in Myocardial Infarction (TIMI) study group, which he chairs at BWH. In the Clopidogrel as Adjunctive Reperfusion Therapy (CLARITY) trial conducted in 319 sites in 23 countries, nearly 3,500 patients received clopidogrel or a placebo in addition to standard treatment.

The TIMI-CLARITY team, led by HMS associate professor Christopher Cannon, looked at how well the drug cocktail opened the blocked artery. More than 90 percent of the patients underwent angiography, and a dedicated, blinded laboratory evaluated blood flow to the heart. The primary

STRETCHING THE LIMITS: Clinical trials at Brigham and Women's Hospital and in China have found that the antiplatelet agent clopidogrel may help extend the lives of people who have suffered major heart attacks.

endpoints of the study were a blocked coronary artery or death or a second heart attack prior to angiography. Clopidogrel was credited with a 36 percent reduction in the odds of these outcomes. The drug also was found to be equally beneficial regardless of which additional drugs were in the clot-busting cocktail, the patient's age or sex, or the location of the heart attack. Bleeding, especially intracranial hemorrhage, is always a risk to be weighed against the benefits of clot-busting drugs, but the TIMI study group found that clopidogrel did not add to the risk of this complication.

Based on this study and a larger trial in China focused on reducing mortality, a decision to include clopidogrel in clot-busting cocktails in the United States is expected soon. Sobotine believes the drug may find use around the world because it is inexpensive, safe, and effective. "For three dollars a pill," he said, "you get this benefit, which is not too different from other interventions costing thousands of dollars." ■

Toi Viinikka is a former intern at Focus.



CRASH OF A TITAN:
Although Caesar's
murder was one of
the best documented
in history, his own
behavior continues
to shroud the event
in mystery.



DEAD MEN TALKING



Did Julius Caesar
stage his own death?
Was King Tut
murdered? And what
killed Alexander
the Great? A forensic
psychiatrist joins
hot debates
over cold cases.

by HAROLD J. BURSZTAJN

JULIUS CAESAR, THE HARUSPICES WARNED, WOULD IGNORE THEIR GUT instincts at his own peril. One morning in early March 44 B.C., these specialists in the Etruscan art of divination carefully peered at sacrificial animal entrails. The signs were troubling. But Caesar would not be deterred from his plan to attend the Senate.

It was not the only dark omen the fabled Roman dictator received—and ignored—in the days preceding his murder. A soothsayer had famously warned him that a grave danger would befall him no later than the Ides of March. Caesar's wife was so disturbed by her dream of their house collapsing that she begged him not to leave that fateful day. And as Caesar made his way to the Senate, someone who had learned of the conspiracy pressed a warning note into the doomed man's hand.

While many historians agree on the chain of events surrounding Caesar's assassination—one of the most meticulously documented murders in history—an intriguing question remains: *why* did this man succumb in the manner he did? Did Julius Caesar—a genius, a shrewd general who never lost a battle, and perhaps history's most brilliant military tactician—really walk blindly into a trap? He had access to high levels of intelligence; he even died with the warning note clutched in his hand. Why did he dismiss his bodyguards shortly before his murder? How could such a wily, well-informed power broker and long-term political survivor come to be killed in front of hundreds of witnesses at a Senate gathering?

DID JULIUS CAESAR—A GENIUS, A SHREWD GENERAL WHO NEVER LOST
A BATTLE, AND PERHAPS HISTORY'S MOST BRILLIANT
MILITARY TACTICIAN—REALLY WALK BLINDLY INTO A TRAP?



A TWIST OF THE KNIFE: Some have suggested that Caesar's final words to Brutus ("Et tu Brute?"), if he really uttered them, hinted at patricide; Brutus's mother had been one of Caesar's many conquests.

When Atlantic Productions, a British-based, award-winning television production company, asked me to participate in its investigation into this puzzle for the Discovery Channel, I couldn't resist. To cover as many angles as possible in its planned documentary—"Who Killed Julius Caesar?"—the company had assembled a team of researchers that included an internationally distinguished forensic criminal investigator and several talented classical historians. This would not be my first foray into the realm of psychohistorical inquiry. I had already served as a forensic psychiatric analyst on another Discovery Channel program, "The Assassination of King Tut."

In the Caesar analysis, I would be applying many of the same tools and principles I had employed on the Tut project. Psychoanalytically informed decision analysis modifies the assumption of traditional decision analysis—that under conditions of uncertainty, humans make choices based on rational self-interest—with the psychoanalytic perspective that "rational" and "irrational" in a given context may not be obvious, commonsensical, or universal. I was intrigued by the chance to apply this type of analysis to the seeming paradox of Caesar's murder.

Body of Evidence

Although the crime took place more than 2,000 years ago in a setting that now bears little resemblance to the imposing complex it once was—today the locals use the ruins of Pompey's portico as a cat sanctuary—substantial and detailed clues remain. The conspirators had not intended to leave such a trail; their original plan, historical sources recount, had been to dump Caesar's lifeless body in the nearby Tiber. The reasons behind the timing and motive of their change of heart remain murky, but all accounts

PYRAMID SCHEME

Of all history's medical mystery controversies, none has raged more fiercely than the question of whether King Tutankhamun's death resulted from natural causes or foul play. Did the 18-year-old boy-king fall victim, as one scholar has proposed, to an infected insect bite? To tuberculosis? To an accidental fall from a chariot? To poison? Or to an assassin's blow to the back of his skull? These are just a few of the many theories that have been advanced over the years.

This spring, the media widely reported that the mystery had finally been solved; King Tut, a team of Egyptian scientists who conducted the first-ever CT scans on his mummy concluded, had not been murdered but had likely died of gangrene that set in following a leg fracture. Yet, while the media presented the team's findings as definitive, not all scholars are convinced.

In my role as a forensic psychiatric analyst on the Discovery Channel documentary, "The Assassination of King Tut,"

I considered a number of people in Tut's inner circle who might have had the motive, means, and opportunity to engineer the young king's demise. The two principal suspects, Ay, Tut's prime minister who succeeded Tut as king and appears to have forced Tut's widow into marriage, and Horemhab, Tut's military commander, who in turn succeeded Ay to the throne, were the *de facto* rulers of Egypt from the time Tut was crowned at the age of nine.

As Tut matured into manhood, he would likely have posed a threat to their behind-the-scenes power. To be a compliant child in need of the protection of a powerful regent might mean something very different than to be an adolescent king eager to take the reins of power from that regent. People will resort to far riskier acts, including murder, to avoid the loss of power than they might simply to gain power. When the question is asked, "Who had the most to lose from Tut continuing to be alive?"

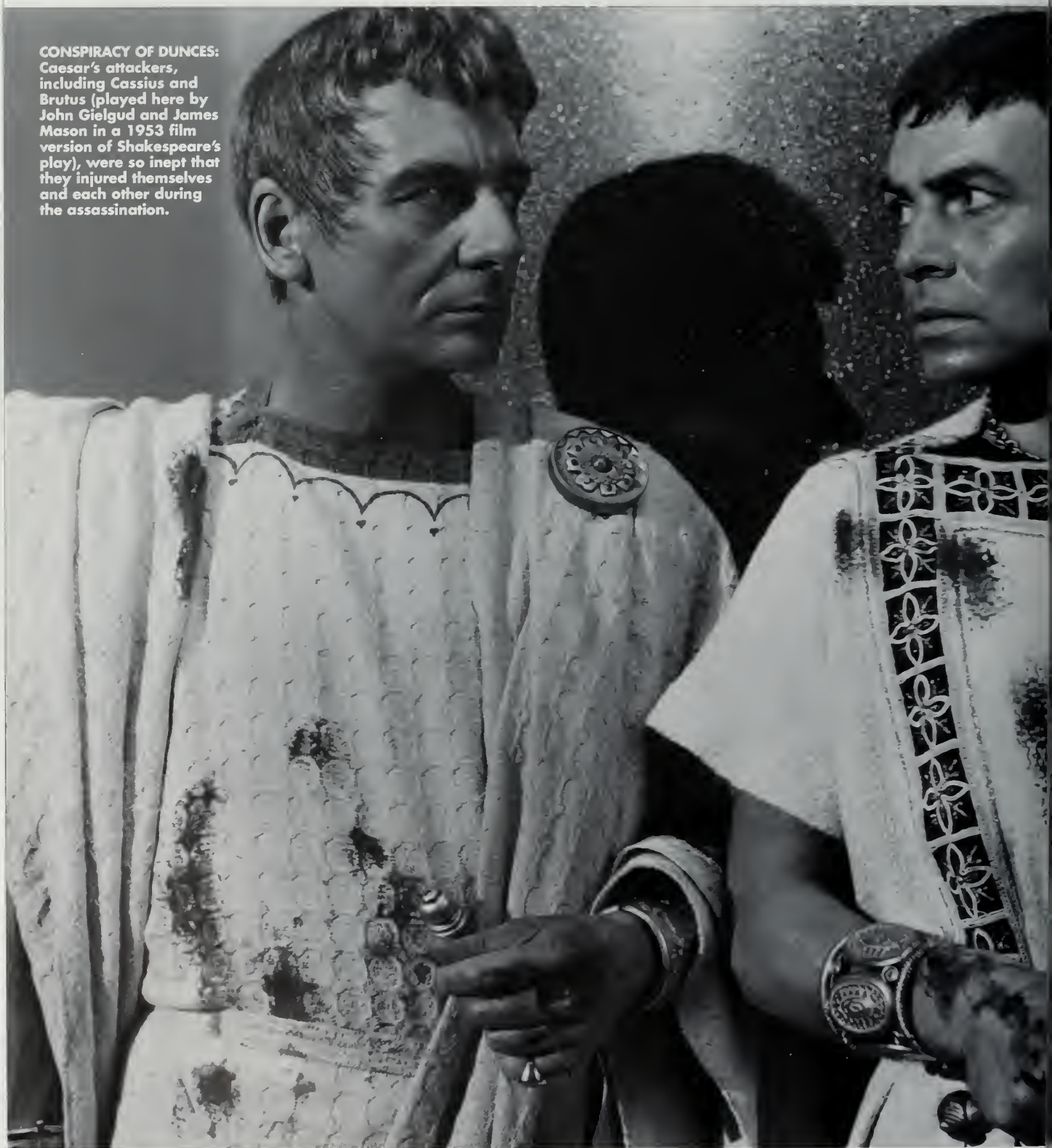
only one suspect leaps out as prime: Ay, whose influence could only diminish as the king came into his own.

Although the Egyptian investigators insist that the physical evidence points away from conspiracy, others are not so sure. Experts continue to disagree about the origin and significance of bone fragments found loose in Tut's skull. Some suspect they resulted from the embalming process itself or from early rough handling of Tut's mummy by archaeologists. To others, they signal evidence of lethal—perhaps deliberate—head trauma. Tut might have been particularly vulnerable to a fall—or a push; some experts have interpreted the x-rays of his mummy as revealing signs of Klippel-Feil syndrome, a musculoskeletal malformation that can make it impossible for those born with the condition to turn their heads without moving the entire torso. Even if Tut suffered from a medical condition that increased his risk of accidental death, that doesn't necessarily mean that his death was an accident.

It is possible that the mystery will never be solved to everyone's satisfaction; the politics of contemporary Egyptology are every bit as complex as the politics of power were during Tut's reign, with many staking out absolutist claims about what remains a case open for analysis. ■



CONSPIRACY OF DUNCES:
Caesar's attackers,
including Cassius and
Brutus (played here by
John Gielgud and James
Mason in a 1953 film
version of Shakespeare's
play), were so inept that
they injured themselves
and each other during
the assassination.



AS I REVIEWED ALL THE EVIDENCE, A SUSPICION BEGAN TO FORM.
MIGHT CAESAR, DRIVEN BY NARCISSISTIC CONCERN FOR HIS OWN IMAGE
AND DIGNITY, HAVE ENGINEERED HIS OWN DEATH?



agree that Caesar's corpse lay sprawled on the spot where the dictator had been cut down for some time before slaves finally transported it to Caesar's household.

Antistius, a doctor who may have been Caesar's personal physician, was summoned to conduct a postmortem examination. According to his autopsy report—perhaps history's first recorded application of medical knowledge to a homicide investigation—only one of Caesar's 23 stab wounds had proved fatal. Although it is impossible to verify Antistius's conclusions—the frenzied crowd at Caesar's public funeral improvised a pyre and cremated the body—his inquiry marked the beginning of the pathologist's role as expert witness to murder.

Given our inability to reexamine the physical evidence, it made sense to extend our investigation in a different forensic direction, one geared toward psychiatric analysis. The Italian detective on the case, Luciano Garofano, was anxious to reassess questions about Caesar's physical and mental conditions in the period leading up to the assassination. Specifically, Garofano sought to understand why Caesar had acted so strangely in the weeks before his death.

We contemplated in particular one instance of Caesar's odd behavior that took place not long before his murder. By 44 B.C. resentment of Caesar was already festering among Rome's powerful old aristocratic elite. He had been named dictator for life, and some citizens referred to him as their king, although Caesar had ostentatiously refused to accept a crown, despite adopting many regal trappings. In January of that year, Caesar's likeness began appearing on Roman coins. This unprecedented, shocking use of the image of a living person fueled suspicions that Caesar, despite his protestations, was planning to overthrow the

republic and declare his reign royal. Rumors swirled that an illegitimate Egyptian son—by Caesar's lover Cleopatra—would succeed Caesar, a prospect that left Rome's aristocracy aghast. When a group of senators went to Caesar—according to some accounts, to placate his ambitions by offering him deification—rather than rising to honor the senators upon their arrival, he remained seated, a grievous insult that may have sealed his fate.

Plutarch claimed that Caesar refused to stand for fear of having an epileptic seizure, while another ancient historian, Dio, suggested that Caesar may have stayed in his seat to prevent an attack of diarrhea. Considering other details in descriptions of his behavior, the question as to whether temporal lobe epilepsy influenced Caesar's choices seemed well worth exploring. Symptoms of temporal lobe epilepsy, which become more common as the seizures progress and become more generalized, include increased dissociation and incontinence of bladder and bowel.

As I reviewed all the evidence, including Caesar's medical history, a suspicion began to form. Might Caesar, driven by narcissistic concern for his own image and dignity, have engineered his own death? Might a man who had risen to become the most powerful ruler in his world have found it deeply humiliating to lose control of both his sense of continuity in space and time and his body in public? It is reasonable to infer that Caesar would have found it far more painful to be perceived as pitiable and incontinent than haughty and rude. The life choices he faced might have struck him as especially stark: old age and increasing fits, temporal lobe-influenced loss of memory, and even public diarrhea—or a dramatic exit worthy of the most powerful dictator the world had ever known.

IT DOES NOT SEEM FARFETCHED TO INTERPRET THESE EVENTS AS THE CAREFUL ORCHESTRATIONS OF SOMEONE WHO, IN WRITING ABOUT HIS LIFE, CLEARLY CRAVED HISTORICAL IMMORTALITY.



HE SHOULD HAVE BEEN A CONTENDER: Caesar named his grand-nephew as his successor, thwarting the ambition of Mark Antony (portrayed here by Marlon Brando).

Suicide by Cop?

I next raised the question of whether Caesar's public murder was not simply a narcissist's suicide, but also a consciously chosen strategic act designed to ensure his succession. One classical historian on our team has argued that Caesar effectively handed the conspirators a deadline when he announced his impending departure for war with Parthia. Garofano noted that Caesar secretly changed his will to name his successor six months before his death—and he left every citizen enough money to live on for three months, guaranteeing a groundswell of mourning and adulation. It does not seem far-

fetched to interpret these events not as the acts of a man blinded to his vulnerability by his own arrogance, but as the careful orchestrations of someone who, in writing about his life, clearly craved historical immortality.

It is one hypothesis but no more than that; I used forensic neuropsychiatry and psychoanalytically informed decision analysis as ways to open other paths of inquiry, rather than to come to a definitive conclusion. As a working psychoanalyst, I exercise curiosity in the most private of settings about an analysand's received truths and accepted "absolute" wisdom, to help free the analysand to ask previously unthink-

able questions. As a forensic psychiatrist, I work on interdisciplinary teams to explore potential translations between the clinical world of meaning and the legal world of objectivity, to understand the choices people make when faced with ambiguity or adversity.

While the circumstances of Caesar's death must remain shrouded in speculation, the aftermath clearly dovetailed with his enormous ambitions. Within a few years, every one of the conspirators would be dead, some by their own hands. The Roman Republic, which the killers had ostensibly hoped to preserve, effectively ended with Caesar's murder. Power passed quickly from the dead dictator to his handpicked successor. Caesar's grand-nephew Octavius was only 19 at the time of his uncle's assassination, but as the chief heir to Caesar's tremendous fortune and powerful family name, he commanded the loyalty of the Roman middle and lower classes outraged by the murder of their champion. He would become Rome's first emperor, known as Caesar Augustus.

Two years later, his dead uncle would be formally deified as "the Divine Julius," and Caesar Augustus would take the title of "Son of God." Every Roman emperor who followed Augustus also adopted Caesar as part of his name until the reign of Hadrian, who designated Caesar as the title of the heir apparent; the imperial use of Caesar would reverberate many centuries after Julius Caesar's death with the German Kaiser and the Russian czar, cementing a legacy of immortality that perhaps even Caesar himself couldn't have imagined. But, then again, Caesar had always gotten everything he wanted in life. Why not also in death? ■

Harold J. Bursztajn '76 has served as co-director of the Harvard Medical School Program in Psychiatry and the Law at the Massachusetts Mental Health Center since 1982. He also maintains a private practice in Cambridge, Massachusetts.

ALEXANDER THE GREAT

Alexander the Great was one of the most powerful military conquerors who ever lived, a daredevil who insisted on personally leading the charge into battle. He founded numerous cities and colonies, was crowned pharaoh of Egypt and king of Persia, and survived war-related injuries and illnesses ranging from hypothermia, to arrow strikes, to a splintered rib and torn lung. Is it possible that this man, one of history's fiercest warriors, succumbed to a broken heart?

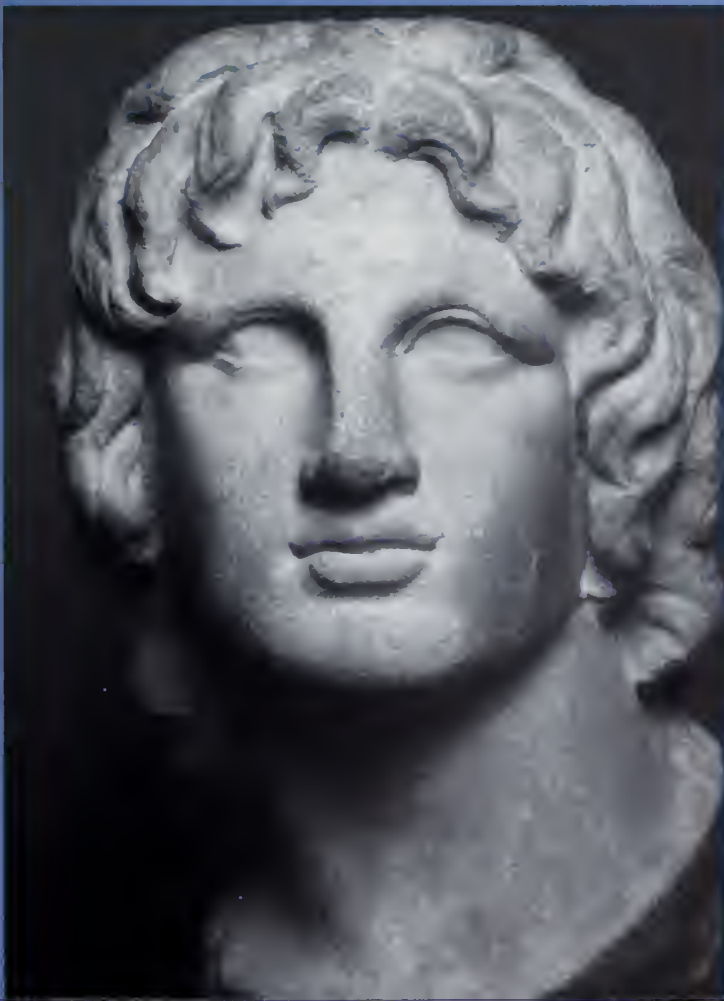
Whispers of regicide swirled when 32-year-old Alexander met his sudden, mysterious end. Ancient chroniclers agree that, following one of his customary bouts of heavy drinking with friends, Alexander came down with a burning fever. His condition deteriorated steadily for nearly two weeks before he died. Scholars have proposed a number of natural causes, including malaria, tuberculosis, influenza, alcoholic liver disease, schistosomiasis, leptospirosis, and even West Nile virus. One infectious-disease expert theorized, in a 1998 *New England Journal of Medicine* article, that Alexander fell victim to untreated typhoid fever, perhaps complicated by ascending paralysis and bowel perforation. Ascending paralysis, which mimics rigor mortis, could explain the odd legend, the author claims, that Alexander's body didn't decay for days after his death.

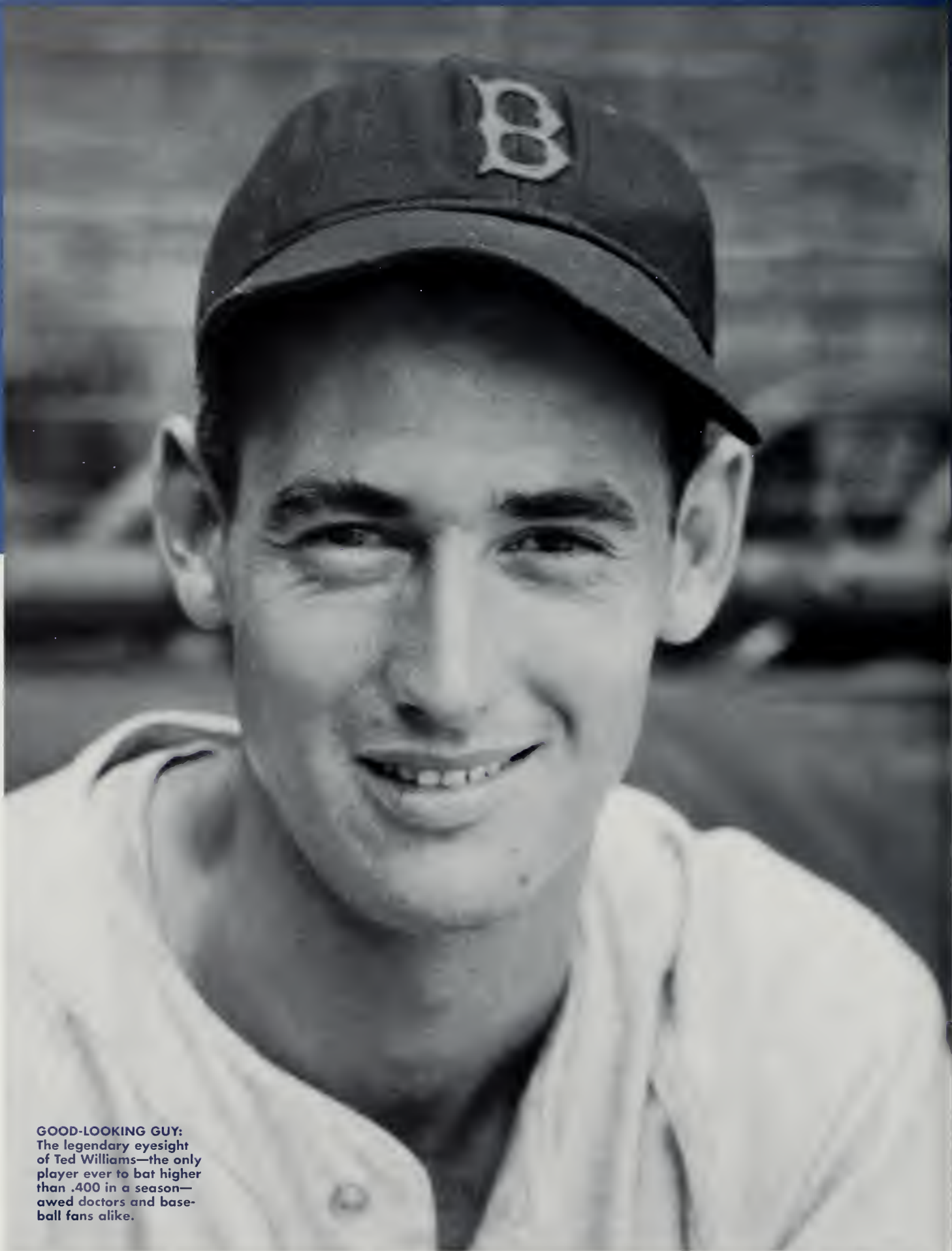
But others have argued that the recorded symptomatology and time course of Alexander's final illness are inconsistent with each of the various proposed diagnoses. Could something more sinister have cut down this battle-hardened young man in his prime? Some have eyed with suspicion the wine Alexander imbibed so heavily, suggesting that it may have contained poison. Certainly, jealousy, ambition, or revenge could have motivated one or more of Alexander's many enemies—as they inspired the murders of Alexander's father, mother, half-siblings, wife, heir, and illegitimate son.

Another theory holds that white hellebore, a plant widely used in ancient Macedonia as a purgative, might have been to blame. Alexander may have made regular use of it, and even a small overdose of hellebore could have proved lethal. Whether hellebore felled Alexander by means of a murderous conspiracy or accidental overdose, or some infectious disease defeated Alexander's immune system, the king's vulnerability may ultimately have been more psychological than physical. As a forensic psychiatric consultant to a third Discovery Channel investigation, I considered that, at the time of his death, Alexander was in despair, figuratively if not literally brokenhearted. Hephaistion—Alexander's second in command, best friend, and lover—had died eight months earlier, perhaps of typhoid fever, or perhaps of poisoning by those resentful of the power he wielded as Alexander's favorite.

Whatever the cause of Hephaistion's death, Alexander is reported to have gone mad with grief, shaving his head and the manes of the army horses, and, legend says, executing the attending doctor, who had failed to save his lover's life. A huge funeral memorial to honor Hephaistion—who, Alexander stipulated, was to be worshiped as a divine hero—was still under construction when Alexander himself died.

Alexander's frenzy may well have led him to self-medicate with alcohol and to take more risks than usual. Did his excessive drinking and staggering grief signal weakness to enemies who decided to take him out? In his zeal to plunge himself quickly back into the distraction of battle, did he unwittingly swallow too much of the purgative that had helped him return to fighting trim in the past? Or did his grief and depression fatally compromise his ability to resist infectious disease? Whatever the immediate cause of death, I think it likely that the loss of Hephaistion, coupled with Alexander's inability to complete the grieving process, marked the beginning of Alexander's spiraling vulnerability to sickness, overindulgence, self-destructive behavior—and perhaps even wicked plots. ■



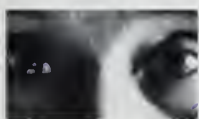


GOOD-LOOKING GUY:
The legendary eyesight
of Ted Williams—the only
player ever to bat higher
than .400 in a season—
awed doctors and base-
ball fans alike.

ONE IN THE BATTER'S BOX—HAVE REALIGNED PERCEPTIONS OF VISION.

view

masters



LEGENDARY RED SOX HITTER TED WILLIAMS REFUSED TO DRIVE IN the left lane of multi-lane highways at night, to prevent oncoming headlights from damaging his vision. Another fabled slugger, Rogers Hornsby, avoided watching movies and reading newsprint for the same reason. And, more recently, when Orlando Cabrera played shortstop for the Red Sox in the seventh game of the 2004 American League Championship series against the Yankees, a pair of goggles bulged in his back pocket during the bottom of the ninth, ready to protect his eyes from the imminent champagne celebration. ■ For baseball players, acuity of vision is essential, as it is for most artists. Yet a surprising number of prominent painters have had abnormal depth perception, leading us to wonder whether this anomaly might actually have proved an asset in the studio. ■ Part of our ability to see three-dimensionally is known as stereopsis, or binocular depth perception, and it exists because our eyes register the world from two slightly different perspectives. As Leonardo da Vinci noted centuries ago, these viewpoints produce two distinct retinal images.

by MARGARET S. LIVINGSTONE AND BEVIL R. CONWAY

DOUBLE DUTCH:
After moving from
the Netherlands to
the United States in
1926, the Abstract
Expressionist master
Willem de Kooning
moonlighted as a
housepainter.



Try this: hold your index fingers up, with one about ten inches from your nose and the other a dozen inches away, directly behind the first. Now look at your fingers out of one eye at a time and you will notice that the two "scenes" vary significantly; through your right eye, the finger farther away is to the right of your closer finger, while through your left eye, the far finger is to the left of the near finger. The greater the separation of your fingers, the greater the discrepancy between the two retinal images. The brain uses the discrepancies between the retinal images—in addition to other monocular depth cues,

such as shading, perspective, and occlusion—to estimate distance and generate a rich perception of depth.

The stereoviewers of the Victorian era and the View-Master toys dating from the 1930s both produce vivid impressions of depth by superimposing two photographs taken from slightly variant positions. Autostereograms—developed in the 1990s under the brand name Magic Eye—are based on the same principle. The Magic Eye images feature a horizontally repeating pattern, which differs slightly with each repetition. When each eye looks at a different part of the pattern, the viewer experiences

an illusion of depth and thus can see three-dimensional images appearing to pop out of two dimensional patterns. If you have normal stereopsis and view an autostereogram with uncrossed eyes, you should perceive an image floating eerily in front of the plane of the paper. Yet some viewers will fail to detect the image, either because they can't voluntarily uncross their eyes and still focus on something, or because their lack of stereopsis prevents them from registering depth.

Stereopsis is just one important cue for depth perception; others include perspective, shading, occlusion, haze,

A person lacking stereopsis might become more sensitive to other, monocular depth cues—precisely those cues artists can render in paintings.

and relative motion. In real life our visual systems integrate all these cues seamlessly, enabling us to interact accurately with our environment. In two-dimensional works of art, such as paintings, though, only the monocular static cues can contribute to the illusion of depth; stereopsis and relative motion reveal the flatness of the canvas. So the next time you find yourself looking at a painting rich in depth cues, stand at arm's length and try closing one eye; you may experience the illusion of entering the painting.

The ability of painters to translate the three-dimensional world into two dimensions is remarkable. Perhaps more astonishing, however, is the curious feat our visual systems perform in enabling us to perceive the visual world as three-dimensional in the first place. The brain's only visual input comes from a pair of two-dimensional images; the retinal images are, after all, flat. Our brains then convert these flat images into a vividly three-dimensional experience

by using the same cues a painter employs, combined with stereopsis and relative motion.

Optical Collusion

Just as stereopsis hampers the viewer from seeing all the depth a painter places onto a canvas, it can also hinder the artist trying to depict three-dimensional scenes on flat surfaces; art teachers often instruct students to close one eye when viewing a scene in order to flatten it. In fact, we suggest that stereoblindness might prove an asset rather than a disadvantage to an artist. A person lacking stereopsis might become more sensitive to other, monocular depth cues, such as shading, perspective, and occlusion—precisely those cues artists can render in paintings.

Only about 10 percent of the population is stereoblind. The most common cause of this condition is an imbalance during infancy in the fine motor control of the six muscles that position the eyes; this produces a mis-

alignment, or strabismus, which can be obvious—as in cross-eyed or “walleyed” people—or so subtle only experts can detect it. When the eyes are misaligned, the brain can not interpret the differences in the two retinal images, and stereopsis cannot develop. Sometimes the misalignment produces double vision. In such cases the brain's solution is to suppress the input from one eye. Eventually this input will wither, and the vision from that eye will become permanently poor—a condition called amblyopia, or “lazy eye.”

Because stereopsis requires precise alignment of the eyes, people with misaligned eyes usually have weak stereopsis or lack it altogether. Poor stereopsis can be diagnosed from a photograph if the image reveals a misalignment of the eyes.

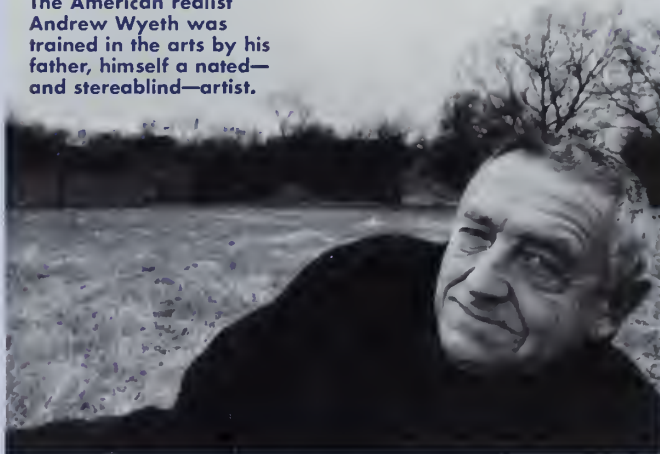


NO KIDDING: In 1939 the View-Master's inventor envisioned his product not as a toy but as a three-dimensional alternative to postcards.

PAINT IT BLACK: In his early “black paintings,” Frank Stella exhibited the precision and rationality that characterized the minimalist art movement.



LIKE FATHER, LIKE SON: The American realist Andrew Wyeth was trained in the arts by his father, himself a noted—and stereoblind—artist.



Most major league baseball players have excellent stereopsis, probably because every bit of visual information can be important in hitting a ball traveling up to a hundred miles an hour.

(Of course, people with normal stereopsis who can voluntarily cross their eyes can mimic a misalignment.) In fact, eye alignment in photographs is the basis for the clinical test of strabismus—the Hirschberg test—in which ophthalmologists compare the relative positions of the light reflections in the eyes. For this test to be reliable, the light source and the camera cannot be too close to the subject, and the subject must be gazing into the distance.

Although the Hirschberg test can reveal ocular misalignment—and thus poor or no stereopsis—it cannot prove that a subject possesses normal stereopsis. First, the poor eye of someone with amblyopia can wander, causing the eyes to align sometimes and misalign at other times—yet at all times the person lacks stereopsis. And second, for unknown reasons stereoblindness can occur even with normal or close-to-normal eye alignment. The best way to evaluate someone's stereoacuity is to test it directly, but when

this is impossible—as in the case of people who have died—then photographs can allow us to assess the likelihood of poor stereopsis.

The photographs of Mickey Mantle and Roger Maris below show aligned eyes—the light reflex registers in precisely the same place on both eyes. Yet the photograph of Babe Ruth reveals misaligned eyes. Ruth's ophthalmologist reported that the Babe was amblyopic; almost blind in his left eye, he likely had poor or no stereopsis.

How could the Bambino have been such a successful slugger without stereoscopic depth perception? Two explanations are possible. One is that he was not amblyopic but rather lost some vision in one eye late in life; his ophthalmologist examined him just before he died. The second is that the Sultan of Swat used other cues to gauge his famous swing. The latter seems likely because photographs often show his eyes as misaligned, even early in his career.

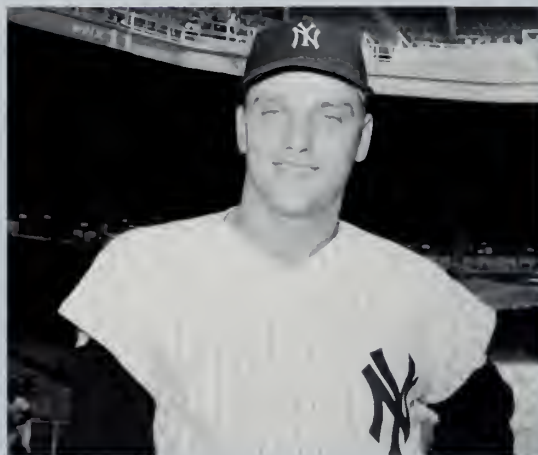
So is stereopsis important in hitting a baseball? Major-league pitches

travel so fast that the ball reaches homeplate in less than half a second, so the batter must decide whether—and then how—to swing at a pitch early in its trajectory, within the first tenth of a second of the ball's leaving the pitcher's grip. Therefore the batter's most important cues are likely to be the pitcher's wind-up and release—and the differences between the two eyes' images at that distance are so small that the information carried by stereopsis is probably negligible. Hitters likely base their swings on such monocular cues as the pitcher's arm speed and the release point.

Most major league baseball players have excellent stereopsis, probably because every bit of visual information, even hints of stereo depth, can be important in hitting a ball traveling up to a hundred miles an hour. And Babe Ruth did strike out frequently. We have even wondered whether he might have developed superior vision in his good eye simply because more visual cortex was



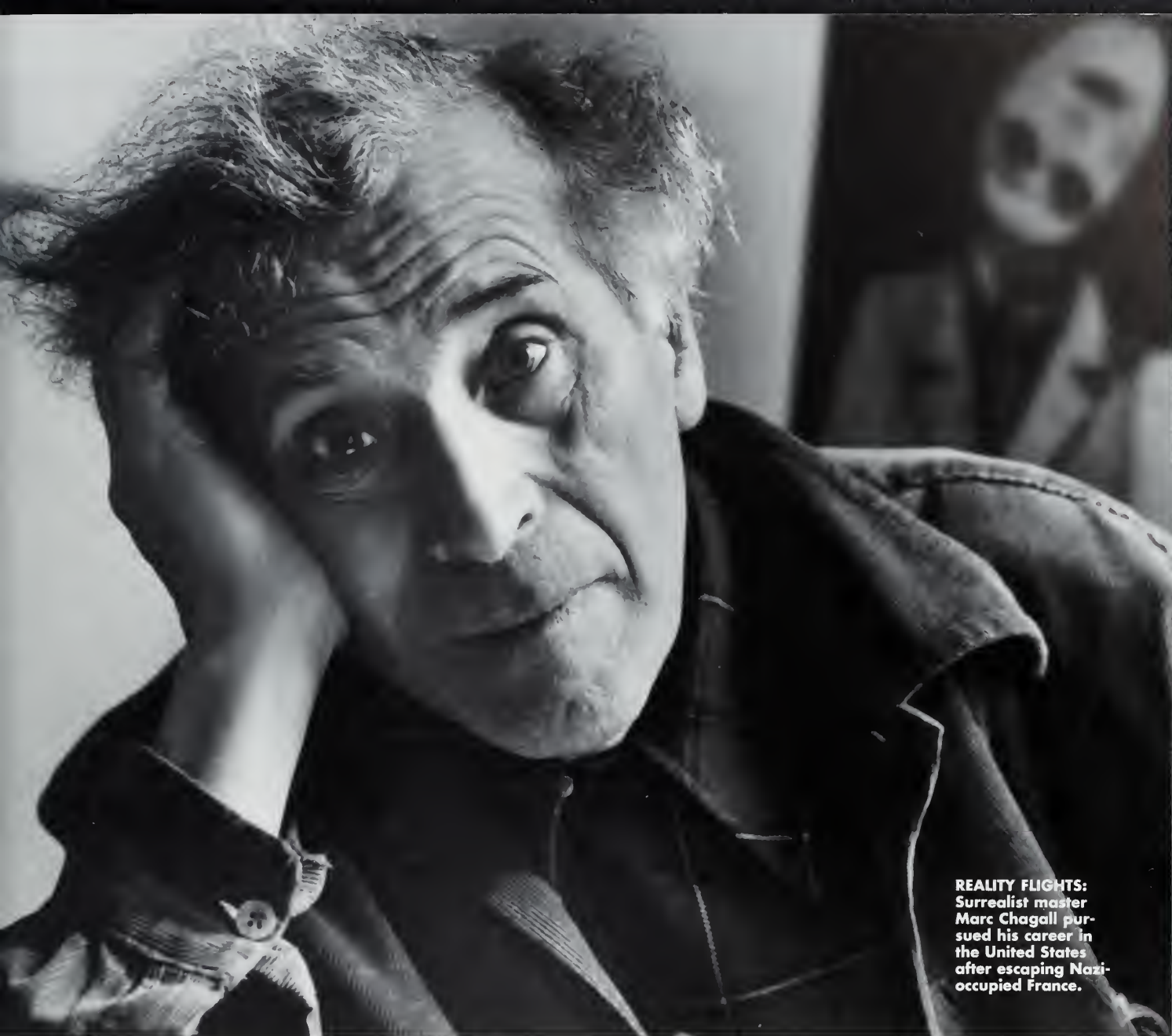
POWER IN PINSTripES: Mickey Mantle was the greatest switch-hitter in baseball history.



THE ARTFUL ROGER: Roger Maris's refined swing helped him break Babe Ruth's home run record in 1961.



THE EMPIRE STRIKES BACK: Babe Ruth's trade to the Yankees is said to have precipitated an 86-year-old curse.



REALITY FLIGHTS: Surrealist master Marc Chagall pursued his career in the United States after escaping Nazi-occupied France.

wired up to it—and this hyperacuity might have made him better at judging the monocular cues about the ball's trajectory. If that's true, we will never have another Babe Ruth because these days you can't make it to the major leagues without excellent vision in both eyes.

Sleight of Sight

It seems logical that artists, like baseball players, would find any visual defect detrimental to their work. Yet, when we looked at photographic portraits and compared the position of the light reflex in the

eyes of 53 famous artists, we found a surprising proportion—28 percent—with misaligned eyes, which would suggest stereoblindness. The artists with ocular misalignment included Marc Chagall, Edward Hopper, Gustav Klimt, Jasper Johns, Frank Stella, Man Ray, Chuck Close, Thomas Moran, Willem de Kooning, Roy Lichtenstein, Alexander Calder, Robert Rauschenberg, N. C. Wyeth, Andrew Wyeth, and perhaps even Pablo Picasso.

Again, because our small survey uncovered so many talented artists with enough ocular misalignment to suggest stereoblindness, we suspect

that poor depth perception might actually enhance the work of artists who want to “flatten” a three-dimensional scene onto a two-dimensional surface. That is, someone who cannot perceive depth from stereopsis may be more aware of—and therefore better able to capture—the other, monocular, cues to depth and distance, such as perspective, shading, and occlusion. Picasso, Hopper, and Wyeth are recognized masters of generating depth-filled canvases based on exactly those cues. At the same time, artists lacking stereoscopic depth perception might tend to accentuate and capi-

PHOTO: PHILIP HAYMAN/WHITMAN ESTATE



RENAISSANCE MAN:
The photographer
Man Ray was also a
painter, filmmaker,
essayist, philosopher,
poet, and leader of
American modernism.

talize on the flatness and surface of a painting, as Klimt, de Kooning, and Stella did.

The Master's Pupil

While diagnosing eye misalignment from a photographic portrait is clinically acceptable, a diagnosis on the basis of a painting ordinarily wouldn't make sense because the artist would have captured the subject's eyes at different times, and the gaze direction could have changed during that interval. Many of Rembrandt's self-portraits, though, show his eyes as consistently exotropic, or turned outward—

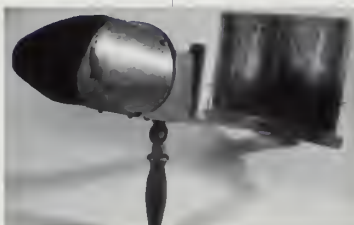
more so than one would expect simply from one eye being painted at a time, and even from the fact that he probably used a mirror and therefore looked slightly rightward when painting his right eye and slightly leftward when painting the left. We wondered whether the relative gaze angle of the eyes in his self-portraits was random, or whether the deviation from alignment was systematic, as it would have been if he were accurately portraying a feature of his physiognomy.

We examined high-resolution images of a collection of Rembrandt's self-portraits spanning his entire career. Many of these paintings and etchings show one eye gazing directly at the viewer and the other eye deviating laterally. We quantified

this pattern in self-portraits in which Rembrandt had articulated both eyes well enough to allow us to gauge the position of the pupil within the opening between the eyelids. Rembrandt portrays his eyes as exotropic in 35 of 36 self-portraits. In 23 of 24 paintings the eye on the right side of the painting looks straight ahead while the other eye deviates outward; in 12 of 12 etchings, this symmetry is reversed.

Because artists make etchings by scratching lines onto a metal plate and then reversing that plate to print an image, what you see on paper is the mirror image of what the artist drew on the plate. The fact that the eye deviating outward in his etchings tends to be opposite from the one deviating outward in his paintings

DOUBLE VISION:
Oliver Wendell
Holmes, HMS
Class of 1836,
helped popular-
ize the stereo-
viewers of the
Victorian age.



The fact that the eye deviating outward in his etchings tends to be opposite from the one deviating outward in his paintings suggests that Rembrandt did have a unilateral strabismus.

suggests that Rembrandt did have a unilateral strabismus; otherwise the deviating eye should be random. Moreover, Rembrandt was not in the habit of painting his subjects with a strabismus: most of his portraits of other people show aligned eyes. The degree of ocular misalignment in Rembrandt's self-portraits is on average ten degrees of visual angle, which would be incompatible with normal stereopsis, and was likely accompanied by poor vision in the deviated eye.

The Tell-Tale Art

Stereopsis is not a prerequisite for artistic talent. Yet the notion that stereoblindness might prove an asset for painters demonstrates the broader possibility that other aspects of brain organization considered detrimental under some conditions might offer advantages

under other circumstances. For example, many talented artists, musicians, mathematicians, and engineers are dyslexic. Some observers have posited that the overrepresentation of dyslectics among artists and musicians represents a compensation for failure in conventional academic fields. Growing evidence suggests, however, that this pattern may be based, in part, on a positive correlation between dyslexia and extraordinary talent.

Our observation that stereoblindness is associated with artistic talent is consistent with the correlation of artistic ability with dyslexia because dyslexia is often associated with poor depth perception and problems with binocular fusion. And of the artists whose eyes we believe were misaligned, at least three—Pablo Picasso, Chuck Close, and Robert Rauschenberg—had severe difficulty learning to read.

Of course, it takes more than visual acuity—or the lack of it—to make an artist or a baseball player great. Such biological factors play out in a cultural arena, inextricably tied to history, motivation, desire, and drive. But understanding the role these factors play can heighten our enjoyment of such wonders as paint daubed on canvas, lines scratched onto metal plates, and baseballs soaring through the air, high above the Green Monster. ■

Margaret S. Livingstone, PhD, is a professor in the Department of Neurobiology at Harvard Medical School and Bevil R. Conway, PhD, is a junior fellow in the Harvard Society of Fellows. They are now collaborating on a study that compares the stereoacuity of art students with that of students majoring in business and other nonartistic fields. Interestingly, Conway has stereoblindness and is, perhaps not coincidentally, an artist.

MASTER IN THE MIRROR: In the self-portrait on the left, which Rembrandt painted in 1633, the eye on the right side of the painting seems to be looking straight at the viewer, but the eye on the left side of the painting seems to be gazing off to the subject's right. Conversely, in the 1639 etching—which is a mirror image—the eye on the left side is looking straight at the viewer, while the eye on the right is deviating outward.



Bewitched, Bothered

HARVARD PHYSICIANS DELVE INTO THE PAST TO



INJUSTICE FOR ALL: Testimony of alleged black magical powers led to the conviction of all accused witches in Salem who did not confess. This lithograph depicts the use of sorcery to levitate books from the judge's bench.

ed, & Bewildered

DIAGNOSE A RANGE OF MYSTERIOUS MALADIES



IMAGE: BETTMANN/CORBIS

PRESENCE OF MALICE: Accusers tilted spectral evidence—in this case a flock of yellow birds hovering over an alleged witch's head—visible only to themselves.



Witches' Brew

FOR TWO DAYS, THE OLD MAN LAY NAKED in the open field adjoining the jail where he and his wife had huddled miserably for the previous five months. He struggled to breathe under the weight of the heavy stones that his fellow villagers had placed, one by one, on a board covering his chest and abdomen. "Do you confess?" the sheriff repeatedly harangued Giles Corey, once even using his cane to force the prisoner's bulging tongue back into his mouth.

But unlike many of the other victims of the 1692 Salem witchcraft hys-

teria, Corey, damned by a teenaged neighbor girl as "a dreadfull wizzard," refused to be tortured into a confession. Given repeated chances to save himself (ironically, those who pleaded guilty and named other names escaped execution, while those who protested their innocence did not), Corey only gasped in reply, "More weight!"

Historians have suggested that what quickly escalated into a tragedy engulfing an entire community may have begun merely as an entertaining way for a small group of bored, impressionable young women and girls from Salem Village to pass a bitter winter. It is perhaps noteworthy that the first two accusers to display mysterious symptoms were also the youngest, children whose Puritan imaginations had been captivated by tales of magical arts told to them

by Tituba, a local servant of West Indian and African descent.

Researchers have advanced various theories, including mass hysteria, conspiracy, and mental illness, to explain how the fascination of a few youngsters could have triggered events leading to the gruesome executions of Giles Corey and 19 others, with more than a hundred imprisoned. One of the most intriguing speculations, put forth by a number of historians, suggests that the origin of the accusers' bizarre behavior, which many in their community perceived as a supernatural affliction, was actually agricultural.

Epidemics of ergot poisoning, labeled "St. Anthony's Fire" in medieval times, have been documented throughout history. According to Alan Woolf, a medical toxicologist and an HMS associate professor of pediatrics at Children's Hospital, people who ingest grain contaminated by the fungus *Claviceps purpurea* can suffer from some of the same unusual symptoms—seeing apparitions and feeling pinpricks, pinches, and burning sensations—described in the records of the Salem trials.

Proponents of the ergot theory, says Woolf, have offered other evidence as well. The weather during the period in question, for example, provided ideal conditions for the growth of ergot on rye. Three of the afflicted girls lived on a farm where ergot-contaminated rye might have flourished, and the records show that several cows in the area died during that time, suggesting a possible infection among the grazing livestock.

And yet a dubious Woolf and other skeptics see many flaws in that toxicological explanation. "A few cows died; so what?" Woolf wrote in a 2000 article on the subject for *Clinical Toxicology*. Moreover, Woolf points out, although some of the girls did indeed display some of the classical symptoms of ergot poisoning, none of them reflected the full constellation of expected signs and symptoms, which would include abnormalities of

And yet a dubious Woolf and other skeptics see many flaws in that toxicological explanation. "A few cows died; so what?" writes Woolf.



the arms and legs due to ergot induced vasoconstriction. Also, unlike those suffering convulsive ergotism, they could stop and start their symptoms on demand. And no evidence of the typical residual effects of ergotism, such as weakness or dementia, ever appeared.

Further scuttling the theory that it was a mycotoxin that fueled the tragic events of 1692, Woolf raises a compelling point: "Other witchcraft trials besides Salem in New England brought 141 persons to trial between 1638 and 1699. Were they all suffering ergotism?"

Woolf believes that the evidence points rather to an emotionally charged web of political motivations, economic jealousies, bitter land disputes, and personal grudges. This climate of festering resentments provided ripe conditions for a tragic settling of scores between disgruntled adults who seized—and were seized by—the powerful fears and emotions stirred up by the girls' odd behavior. On the dark January 1692 day when nine-year-old Elizabeth Parris and eleven-year-old Abigail Williams first began to startle those around them with fits of blasphemous screaming, convulsive seizures, and trance-like states—soon to be imitated by a number of their peers—they probably could not have imagined, in their childish way, the deadly campaign their subsequent babble of witches' spells and demonic trafficking would soon unleash on their community.

And yet they had to live with the sobering legacy of their experience. Some 14 years after Giles Corey died for his stubborn refusal to yield a confession, one of his original accusers, Ann Putnam, by then a 26-year-old woman, offered a confession of her own: "It was a great delusion of Satan that deceived me in that sad time," admitted Putnam in a statement she asked her minister to read aloud to the congregation one Sunday, "whereby I justly fear I have been instrumental to bring upon myself and this land the guilt of innocent blood." ■

Stars in His Eyes



HEN VINCENT

van Gogh began painting a starlit sky one night, he found that "putting little white dots on a blue-black surface" failed to capture the vision before him.

"It often seems to me that night is still more richly colored than the day, having hues of the most intense violets, blues, and greens," he later wrote. "If only you pay attention to it you will see that certain stars are citron yellow; others have a pink glow; or a green blue and forget-me-not brilliance."

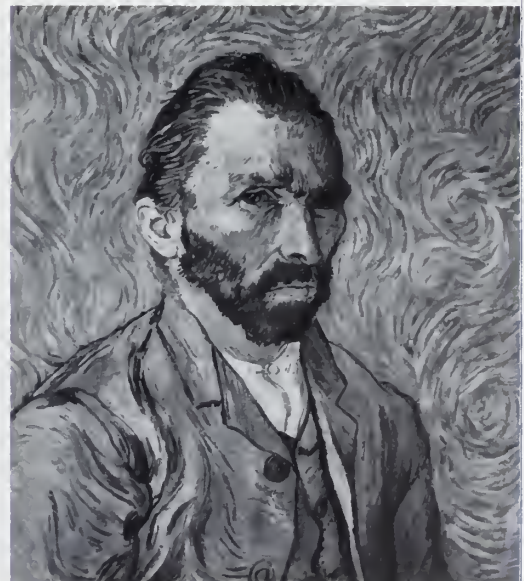
It was the artist's sensitivity to the nuances of hue that first drew Shahram Khoshbin, HMS associate professor of neurology at Brigham and Women's Hospital, to van Gogh's work. As a fine-arts student in Beirut, Khoshbin wrote his senior thesis on the painter's florid use of tertiary colors, which emerge when a secondary color blends with a primary color.

"Through years of experimentation, van Gogh had discovered he could pair certain colors—such as blue-violet with yellow orange—to evoke emotions," says Khoshbin. "Such color combinations can trigger autonomic responses in viewers. When you stand before many of his paintings, your palms turn sweaty, your breaths come rapidly, and your heartbeat quickens."

Despite his passion for art, Khoshbin ended up turning to medicine instead. Soon his growing fascination with neu-

rology led him to ponder van Gogh's behavior as well as his art. Dozens of diagnoses—from schizophrenia, to bipolar disorder, lead poisoning, and absinthe toxicity—had already been advanced to explain van Gogh's vibrant paintings, eccentric life, and dramatic death. While a medical student at Johns Hopkins, though, Khoshbin seized the chance to ask the late Norman Geschwind '51, a pioneer in behavioral neurology who was at Hopkins to give a lecture about Fyodor Dostoevsky, about van Gogh's diagnosis. "That's simple," Geschwind replied, "he had epilepsy—just like Dostoevsky."

Khoshbin felt surprised, even after he learned that van Gogh's own doctor had diagnosed the artist with epilepsy, because he doubted the disease could account for the full range of van Gogh's symptoms. But an incident the following year made that diagnosis resonate after all. While volunteering in an art-therapy studio, Khoshbin noticed that few of





the patients used tertiary colors in their gouache paintings. One evening, as he was helping the janitor tidy the studio, he mentioned his observation. The elderly man walked him downstairs to a custodial closet filled with brooms, mops, and the rustling sounds of nesting rats. There the janitor pulled out boxes and boxes of artwork he had collected over the decades. On the back of each of the hundreds of paintings he had inscribed the artist's diagnosis.

"The schizophrenics' artwork was meticulous and detailed," Khoshbin remembers. "The depressed patients had splashed black and brown everywhere. But what stunned me was the box filled with art by the epileptics: in almost every painting they had used tertiary colors."

Years later, while working with patients who had suffered damage to the temporal lobe, Khoshbin discovered that they perceive colors as being brighter

and images as more vivid than other people do. "Sensory integration takes place in the temporal lobe," Khoshbin says, "so it's easy to understand how a disturbance in that part of the brain can create a different sensory experience."

Khoshbin now believes van Gogh suffered from not just temporal lobe epilepsy, but also a personality disorder associated with it, dubbed the Geschwind syndrome; in the early 1970s, Geschwind had identified a constellation of five personality traits: hypergraphia, or voluminous graphic output; hyper-religiosity; unstable sexual behavior; intermittent aggressiveness; and clinginess.

Van Gogh exhibited all five traits. His hyper-religiosity, for example, once led to his being fired from his job as an evangelist minister for "excessive zeal." He alternated between periods of hypersexuality and hyposexuality and between liaisons with women and with

men. His stormy relationship with the painter Paul Gauguin illustrated not only his clinginess—Gauguin bemoaned the difficulty of ending conversations with van Gogh—but also his aggression. It was just after threatening Gauguin with a razor that van Gogh famously lopped off part of his own earlobe and presented it with much flourish to a young lady of the night.

Dramatic, too, was van Gogh's hypergraphia. A largely self-taught artist who didn't start painting until the age of 27, he nonetheless created more than 2,000 works of art before his suicide a decade later. The year he described the vibrancy of colors in the night sky—and painted his masterpiece *Starry Night*—in fact, was so fertile he was producing, on average, a new painting, watercolor, or drawing every 36 hours. When he wasn't clutching a paintbrush or stick of charcoal, he was grasping a pen, writing long letters far into the night.

Those letters reveal much about van Gogh, from his obsession with color to his instincts for the divine. "When I have a terrible need of—shall I say the word—*religion*," van Gogh once wrote to his brother Theo, "then I go outside in the night to paint the stars." ■

A Long Day's Journey into Night



ONE DAY, WITHOUT warning, Eugene O'Neill's hands jerked, causing the 55-year-old playwright to splash coffee on himself. He then burst

into a fit of weeping, the result not of the accident, he wrote, but of a "nervous impulse."

By that time, O'Neill, the only native-born American dramatist ever awarded a Nobel Prize for literature and the winner of four Pulitzer Prizes, had already been suffering for years from an array of mysterious symptoms. His handwriting had become micrographic, his gait

unsteady, his limbs uncoordinated, and his speech impaired, all of which had a crippling impact on his life and art.

Although O'Neill had been diagnosed with Parkinson's disease a dozen years before his death at the age of 65, an autopsy performed by the late E. P. Richardson, Jr. '43A, revealed a more surprising neuropathology, which he kept confidential at the family's request.

"I helped him. We tore up all the manuscripts together, bit by bit. It took hours...It was awful. It was like tearing up children."



Decades later, Richardson and Bruce Price, an HMS assistant professor of neurology and chief of neurology at McLean Hospital, secured permission from O'Neill's surviving grandchildren to publish the postmortem findings. Their report appeared after Richardson's death in the April 13, 2000, issue of *The New England Journal of Medicine*.

According to the report, O'Neill first noticed a tremor in his hands while a freshman at Princeton University, but it did not affect his writing until he was 41. Two years later, O'Neill noted in his diary his difficulty in controlling a pencil. His tremor continued to worsen so that by 1943, he stopped keeping his work diary because the physical process of writing had become torturous.

That same year, when someone commented on the shrunk quality of his handwriting, O'Neill explained, "There is a physical reason for that—the curse of Parkinson's disease—it's easier to control tremor in minute writing." But, he added, what most disturbed him were the "fits of extreme melancholia that go with it. God knows I have had enough of Celtic Twilight in my makeup without needing any more of the same. And this isn't the same. It isn't sadness. It's an exhausted, horrible apathy."

O'Neill's wife, Carlotta, described days when he could produce no more than a tremulous, illegible scrawl. "No one could read it but me," she later recalled, "and I would type his manuscripts over and over for him. I nearly went blind." Her husband added, "Now, Mrs. O'Neill, who has typed all my plays for years, has to operate with a magnifying glass and a book on Egyptology."

Neurological examinations of O'Neill disclosed poor articulation in his speech and hypotonia of his muscles. His head and torso swayed, even while seated, unless held steady by his arms. Although his gait was wide with irregular foot placement, his posture remained erect. He exhibited no symptoms of

dementia. Then, in 1952, O'Neill's symptoms rapidly worsened; he had difficulty swallowing, became sullen and reclusive, and finally, a year later, contracted a fatal case of pneumonia.

The autopsy revealed an unscathed substantia nigra in the brainstem—the region most affected by Parkinson's disease. The playwright suffered not from Parkinson's, Richardson concluded, but rather an idiopathic form of late-onset cerebellar atrophy, with extension into the anterior lobes of the cerebellum.

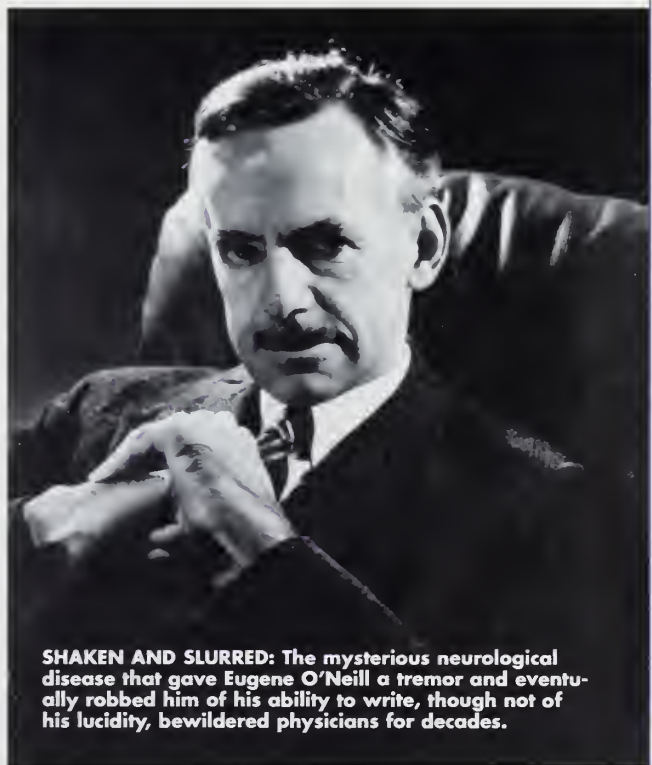
Although O'Neill himself and many of his biographers suspected that his early alcohol binging might have caused his neuropathology, the *New England Journal of Medicine* article argues strongly against it. When alcoholism results in cerebellar degeneration, poor nutrition and chronic abuse are at the root. In this case, however, the authors write that O'Neill's personal records reflect an adequate diet and suggest that O'Neill did not drink to excess for at least 25 years before his death and not at all during his last eight years. Other postmortem findings—a normal liver and testes, organs frequently damaged by chronic alcoholism—strengthen the argument against alcoholism as a factor in O'Neill's disease.

The report does not rule out a genetic etiology—O'Neill's family history hints at an essential tremor in his mother, a brother, and his older son—but the age and paucity of tissue specimens precludes DNA analysis.

Two decades before his death, O'Neill conceived the idea of a cycle of 11 plays intended as a critique of American civiliza-

tion, caught, as he saw it, between its professed democratic ideals and the greed that fueled its progress. Plagued by his worsening disabilities, he completed only two plays, *A Touch of the Poet* and *More State-ly Mansions*, in the proposed cycle. In the year before he died, O'Neill burned the remaining unfinished manuscripts. His wife described the tragic scene: "He could only tear a few pages at a time, because of his tremor, so I helped him. We tore up all the manuscripts together, bit by bit. It took hours...It was awful. It was like tearing up children."

"Had O'Neill been able to fulfill his vision," Price says, "the cycle of plays might have become one of the most extraordinary works of American theater. Instead, his neurological illness stole his abilities and his life, depriving us all." ■



SHAKEN AND SLURRED: The mysterious neurological disease that gave Eugene O'Neill a tremor and eventually robbed him of his ability to write, though not of his lucidity, bewildered physicians for decades.



AN APPETITE FOR MISADVENTURE: Baron Jan Gerrit van Wassenauer was celebrated for his command of the Dutch fleet—but not of his appetite.

THE CURIOUS CASE OF THE INCURABLE EPICURE

The sudden, baffling death of the grand admiral of the Dutch fleet handed a premier physician a mystery—and medical immortality.

by ANTHONY S. PATTON



AUTUMN WIND AND RAIN LASHED HERMANN BOERHAAVE'S CARRIAGE AS IT HURTTLED down dark village lanes and past sodden fields on its rush to the nearby castle. There the doctor found the grand admiral of the Dutch fleet, the Baron Jan Gerrit van Wassenaer, slumped at the edge of his bed, pressing his belly into his lap and groaning. A trio of servants hovered to help prop the admiral in a sitting position. ■ When Boerhaave approached his patient just past midnight on October 30, 1723, the admiral struggled to raise himself and offer his hand, but his pain grew too sharp. Speaking proved agonizing as well, so his son's tutor hastened to provide the details.

"ALL HOPE SEEMED TO BE DIMINISHING. WE WERE HORRIFIED AND STUPEFIED AT THE OCCULT NATURE OF THIS UNIQUE MALADY."



During the previous week, van Wasse-naer had suffered a particularly vexing bout of his usual stomach trouble. After three days of near fasting, though, he had felt well enough to treat himself to a sumptuous lunch. He tucked into veal soup and cabbage boiled with mutton, then devoured calf sweetbreads, spinach, a generous helping of duck, two larks, apple compote, and bread, all washed down with beer. Moselle wine had accompanied his dessert of pears, grapes, and sweetmeats. After a brief rest, he joined his son for a horseback romp across his estate.

By the time the admiral returned to the castle, he was feeling ill. To induce vomiting—his customary cure for an upset stomach—he gulped several glasses of tepid water blended with musk thistle extract and perhaps ipecac root extract as well. When the concoction failed to produce results, the admiral swilled four more glasses.

This remedy proved unwise. The admiral began vomiting violently. Suddenly he emitted a piercing howl. When alarmed servants rushed to his chamber, they found him doubled over. Something at the top of his stomach felt torn, he gasped out, and death would soon follow. He asked his servants to lower him to his knees so he could surrender himself to God. While he prayed, his body began to shake violently. Cold sweat formed, and his pulse turned thready. His servants lifted him to his hunched position again. Over the next few hours they warmed him with hearth-heated blankets, moistened his head and chest with the juice of crushed herbs, made him choke down several ounces of olive oil, and offered him medicated Danzig beer.

During these ministrations, the admiral's family summoned James de Bye, a highly respected physician from the Hague. The doctor gave his patient soft pisans of oats to swallow; he also prescribed a milk-and-corn preparation to

be rubbed gently over the chest and abdomen. No tonic provided relief, though, and the grand admiral, surrounded by family members and servants, remained doubled over in agony.

Close to midnight, the admiral's brother, James, also a powerful baron, galloped through the storm to the nearby city of Leiden. By the time he reached Hermann Boerhaave's imposing residence, he was in tears. His brother's last hope lay with the world-famous physician's ability to diagnose and treat the admiral's mysterious ailment.

Cultivating Genius

In 1575, after Leiden gained fame for its brave stance against a Spanish siege, William I, Prince of Orange, rewarded its citizens for their courage by granting a charter for a university. Leiden University soon grew into one of the finest academic institutions in the world, with a celebrated medical school. Benjamin Waterhouse, one of the three original faculty members of Harvard Medical School, trained there in the early 1780s.

Heading Leiden's medical school at the time of the admiral's woes was Boerhaave, whose stature as a clinician and scientist had reached unparalleled heights. Letters from Asia addressed loosely to "The Best Doctor in Europe" arrived on his doorstep. He wrote brilliant books on chemistry and medicine and, following the examples of Hippocrates and Thomas Sydenham, revived the lost art of clinical teaching at the bedside.

Boerhaave trained scores of physicians from all over the globe, including the founders of Edinburgh's influential medical school. He was one of the first to use the microscope and thermometer as tools of medicine, and his description of glandular function remains valid to this day. At one time he was a fellow of the Royal Society of London, a fellow

of the French Academy of Sciences, and chairman of the Surgical Guild in Leiden—quite a feat for a non-surgeon.

Although he had originally intended to become a Calvinist minister like his father, Boerhaave had become transfixed by the works of Spinoza, Descartes, and other philosophers whose ideas clashed with the tenets of the Dutch Reformed Church. So he abandoned his ecclesiastic ambitions and earned instead a medical degree with distinction. He wrote his thesis on the value of fecal examination in the diagnosis of disease.

Boerhaave opened a small medical practice in Leiden, taught private courses out of his home, and began lecturing at the university. His classes proved so popular—noblemen often hired men to arrive at the classroom early and reserve seats for them—that university officials offered him the first opening on the permanent faculty: a professorship in botany. Boerhaave had little experience with the subject but soon mastered it with the aid of the university's extensive gardens, where exotic plants from all over the world flourished. He wrote a seminal text on botany and later trained the noted Swedish scientist Carl Linnaeus, whose plant classification system remains in use today.

The fame of Boerhaave's extensive talents allowed the admiral's desperate family to cling to a shard of hope as the doctor's carriage hurtled to the castle that dismal night.

Eat, Drink, and Be Buried

Boerhaave found his patient in dire straits, though some clinical signs were surprisingly normal: The admiral had no fever. His face had retained its natural color and his eyes their luster. No noxious odor emanated from his breath. When he managed to speak, his voice sounded clear. Yet his pulse remained weak. Despite the many liquids poured into his body, he produced not a single

drop of urine. And his pain felt lacerating. Boerhaave had attended to the admiral's gout over the years and knew him to be a good-humored man who bore discomfort stoically. Even as the admiral tried to stifle his groans, it became clear this was no ordinary affliction.

One of Boerhaave's immediate suspicions centered on poisoning. Few people in the Netherlands enjoyed greater stature than the grand admiral. Beginning in the 1650s, the country had maintained the world's largest merchant fleet. The navy not only provided protection for the commercial ships, but had also been embroiled in innumerable wars with Spain and England. Overseas treaties and alliances, sometimes unsavory, required a corps of expert sailors, and many members of the baron's influential family had served in successful expeditions and battles. Although foreign intrigue and assassination plots were common, motives aside, no poison Boerhaave knew would provoke the admiral's constellation of symptoms.

In those long hours of attending to van Wassenaer, Boerhaave reviewed all he knew about his 51-year old patient. In his youth, the baron had led an active life, filled with sport and horseback riding. As he aged, though, the many diplomatic conferences and lavish parties caught up with him, and he seemed unable, Boerhaave noted, to "observe the exacting niceties of moderation." Indeed, the admiral's voracious appetite had brought him infamy, as he consumed enormous portions of food while drinking prodigious amounts of wine and beer at each meal. The baron himself suspected that his excesses likely caused his chronic gout and the intermittent inflammation of what Boerhaave described as "the mouth of his stomach."

But this latest episode of illness was clearly far graver than any the baron had previously experienced. Boerhaave tried a range of remedies. He bled the

admiral, gave him a goblet of wine to drink, applied a lukewarm preparation of flour and milk to the painful areas, and offered him a concoction made from wild poppies. Yet nothing alleviated the patient's suffering. "All hope seemed to be diminishing," Boerhaave later wrote. "We were horrified and stupefied at the occult nature of this unique malady."

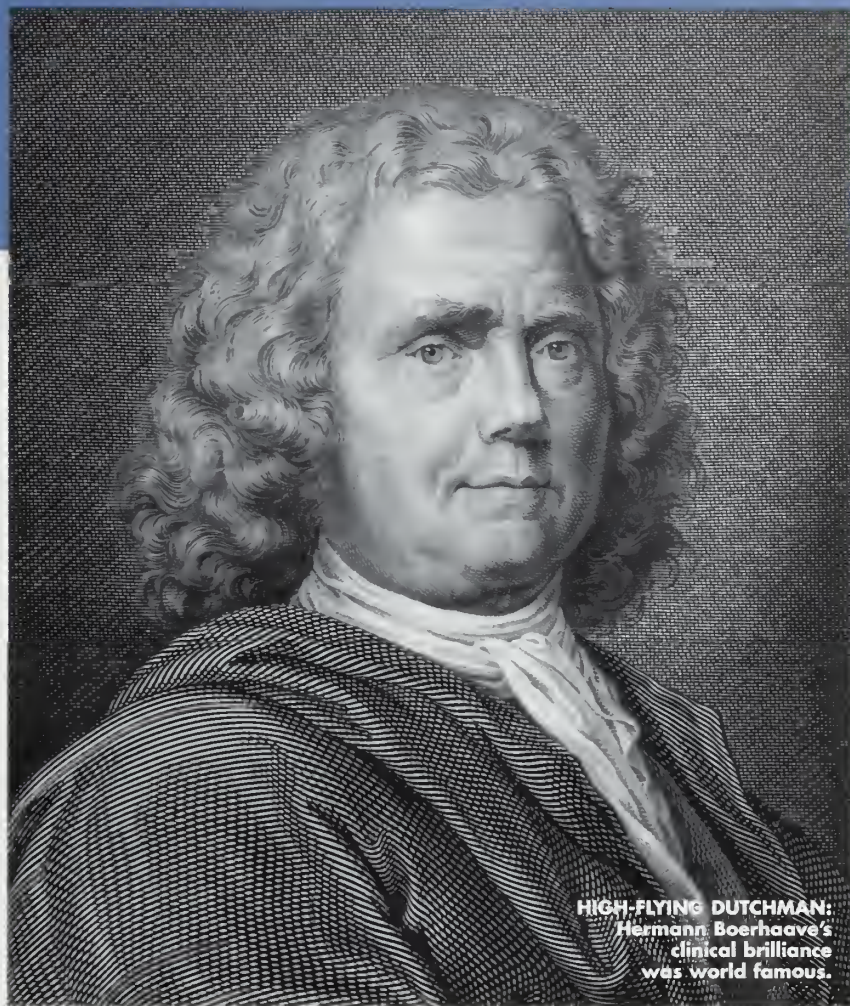
In the late afternoon, Boerhaave noted that the skin covering the admiral's chest and upper abdomen had become swollen with an odd, spongy fluid. Suddenly the patient's already excruciating pain increased. His skin grew cold and sweaty, and slowly, like a wounded ship in his fleet, the admiral rolled onto his side and sank into unconsciousness, never to awaken again.

Internal Review

Like any great scientist, Boerhaave tried to learn from his failure. In elo-

quent Latin, he recorded in detail the history of the patient's illness, including the copious amounts of rich food, beer, and wine the admiral had consumed; his howl of pain; the doctors' ineffectual remedies. Boerhaave catalogued each symptom as well: the baron's swollen epigastrium, the strange crepitus in his skin, his falling urine volume, his weakening pulse, and then his final moments of torment, unconsciousness, and death.

Mystified, Boerhaave agonized over both his inability to render a diagnosis and his unsuccessful treatment. He worried that he and de Bye had possibly exacerbated the baron's misery. Boerhaave himself, following an attack by a swarm of bees, had suffered a painful ulcer in his thigh for five years while a teenager; his biographer, Samuel Johnson, wrote that the ulcer "defeated all the art of the surgeons and physicians, and not only afflicted him with most excruciating pains, but exposed him to



HIGH-FLYING DUTCHMAN:
Hermann Boerhaave's
clinical brilliance
was world famous.

"WELL, WE HAVE ANOTHER BLOKE WHO HAS OVERDONE AND RUPTURED HIS SWALLOWING TUBE JUST LIKE THAT DUTCH ADMIRAL."



such sharp and tormenting applications, that the disease and remedies were equally insufferable." Boerhaave ultimately rejected the received wisdom of his doctors and cared for himself by applying salt and urine to the stubborn wound. Later, when he entered medicine, he resolved never to exacerbate his patients' suffering.

When the admiral died, the two physicians at his bedside agreed that a postmortem examination was essential. "What Doctor is there," Boerhaave later wrote, "who while he treats a disease unknown to him, might be at ease until he had clearly perceived the nature of this disease and its hidden causes?" Aided by candlelight, he undertook the autopsy himself, with several men in attendance, including de Bye, the tutor, and the local minister.

Boerhaave's knowledge of anatomy was extensive; he had long ago mastered Vesalius's work. As a good pathologist, he first described the appearance of the corpse, noting the strange accumulation of fluid in the flanks and the spongy crepitation from air under the skin. When Boerhaave opened the abdomen he felt—and heard—a great rush of air but could find no perforation of the bowel, only generalized distension with a normal liver and spleen. As soon as he nicked the stomach he again heard a loud hissing sound as air escaped; he was astonished to find the stomach empty but for a peculiar dark fluid.

When he next opened the thoracic cavity he immediately felt more air and detected the strong odor of duck. The viscous nature of the dark fluid that bathed the lungs, heart, and mediastinum suggested the olive oil that de Bye had administered to soothe the patient's pain. With deeper dissection, Boerhaave found a ragged communication between the pleural cavities. Then, at the bottom of the chest, he found his answer: a hole in the baron's esophagus,

just above his diaphragm. From above and below, Boerhaave poked his forefinger through this hole into the esophageal lumen, then invited his audience to do the same. He could detect no sign of chronic ulceration or inflammation, but a fresh injury resulting in massive contamination of the pleural cavity by food, saliva, and stomach contents.

Boerhaave had thus uncovered the first recorded case of an esophageal rupture due to forceful vomiting. He speculated on the stresses caused by retching and the quick regurgitation of a large amount of stomach contents into an esophagus. He realized that the esophagus, lacking the serosa, or tough outer layer, that protects the bowel, is prone to blowout. His mechanistic view concluded that compression of the lungs had led to the admiral's death; we know now, however, that the chemical and bacterial injuries can play as important a role in such cases.

Boerhaave's published booklet about the admiral's demise, "*Atrocis, nec Descripti Prius, Morbi Historia*," or "History of a Grievous Disease Not Previously Described," became a classic, perhaps the first complete clinical-pathological correlation of medical history with physical examination, diagnosis, disease progression, and autopsy findings. Its narrative reveals much about the times, including the role of the doctor and the state of medical knowledge. It also marks the significance of the case for all physicians, for without early treatment, patients with esophageal ruptures can suffer long, agonizing hospitalizations and, until recently, most died.

Savings Accounts

Boerhaave's prediction that no one would ever survive the syndrome named after him proved correct for more than two centuries. But in 1947 Norman Barrett, a famous surgeon at St. Thomas's Hospital in London, was

able to save a patient with an esophageal rupture. Since then, thoracic surgeons have remained alert to symptoms of Boerhaave's syndrome. To diagnose the condition quickly and initiate immediate, lifesaving repair can establish a surgeon as a hero; to miss the diagnosis and lose a patient can create a legacy of shame.

When I met Barrett in the early 1960s, the distinguished surgeon told me he considered that groundbreaking case to be one of his proudest moments. At the time I was working at a regional thoracic surgical unit in Devonshire, England, where I, too, faced my earliest challenges with the syndrome. Two years in a row the owner of The Rock, a favorite local pub for vacationing Londoners, rang me up on Boxing Day, the day after Christmas.

"Is this the registrar?" he bellowed into the ancient phone each time. "Well, we have another bloke who has overdone and ruptured his swallowing tube just like that Dutch admiral. I'm sending him over." The pubkeep had become an unofficial expert on Boerhaave's syndrome. Fortunately, our surgical team was able to repair both cases. We found the tear exactly as Boerhaave had described—just above the esophagogastric junction—and were able to suture it within several hours of the injury.

Upon leaving England, I started a surgical practice north of Boston, where I saw many cases of ruptured esophagi. I remember one middle-aged man, a master electrician, who was transferred to our unit from another hospital in severe pain. His diagnosis had baffled his doctors, but my close reading of Boerhaave's account and my experience in England led me to conduct emergency surgery. After the operation I went out to talk to the patient's wife. I'd had little time for explanation beforehand, so I took my time in describing her husband's initial plight and expressing my optimism for a successful outcome.

A T R O C I S,
 N E C D E S C R I P T I P R I U S,
 M O R B I
 H I S T O R I A. •
 S E C U N D U M M E D I C A E
 A R T I S L E G E S C O N S C R I P T A
 A B
 H E R M A N N O B O E R H A A V E.



LUGDUNI BATAVORUM,
 Ex OFFICINA BOUTESTENIANA.
 M D C C X X I V.

"Good God," she exclaimed. "Ruptured his esophagus!" She paused, grabbed my hands, and added ruefully, "That man, he's always doing to excess." Interestingly, he too had tried his own

remedy for gastric distress—a big gulp of baking soda.

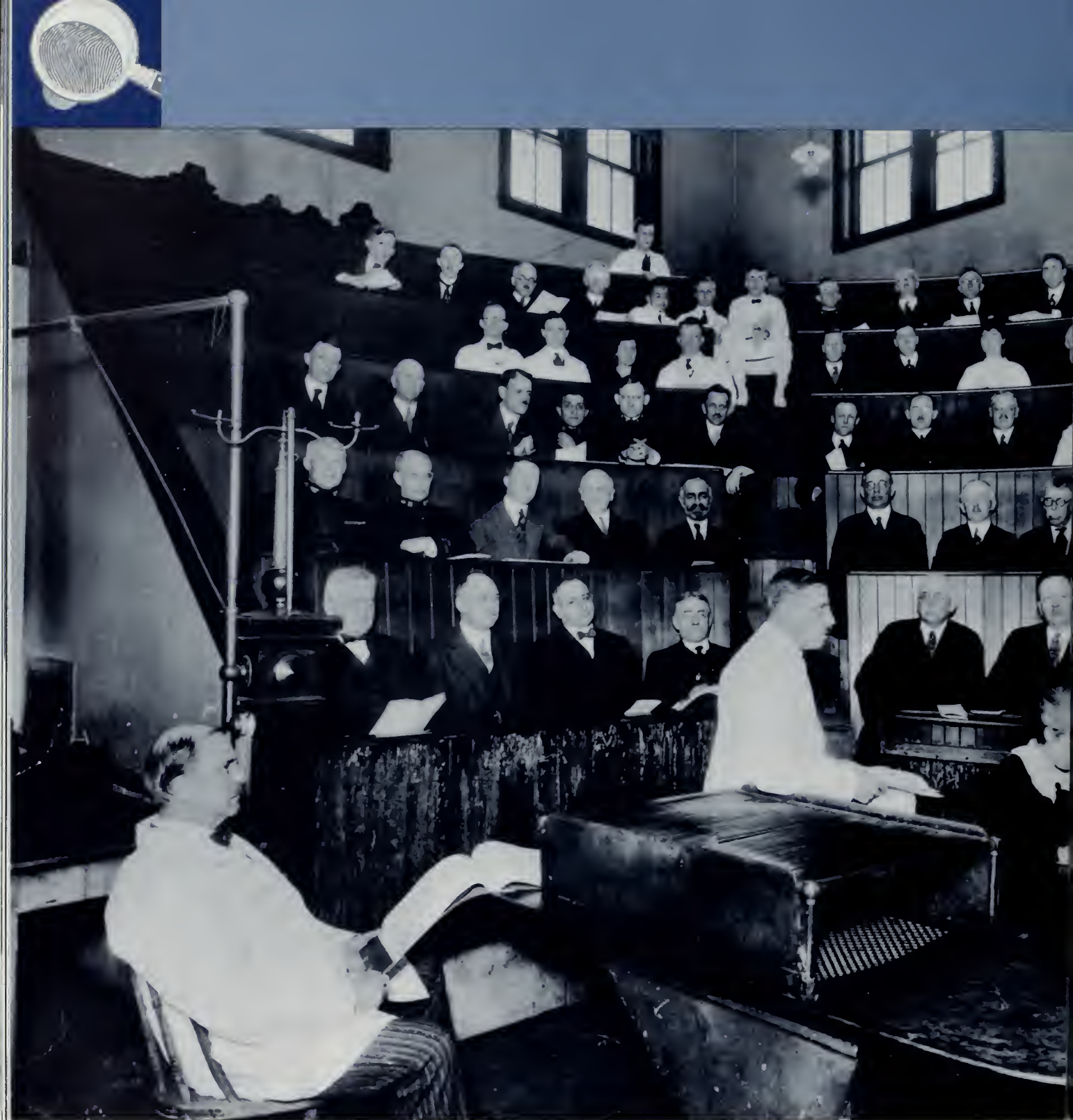
Later in my career, I called numerous patients back for study and ordered barium swallows to see how their repaired

esophagi now appeared. I was amazed at how many of them still had tiny slivers of leaks or thin diverticuli that nevertheless had healed well enough to cause no trouble. Perhaps Boerhaave was right in his original report: no case will ever be completely cured.

Not all cases are as dramatic as that of the admiral, so physicians must remain alert for unusual presentations of Boerhaave's syndrome. Although almost all cases involve vomiting and air either under the skin or in the pleural space, many have more subtle presentations. The vomiting is sometimes triggered by bowel obstruction, severe esophagitis, or even seasickness. Today surgeons can save the patients whose diagnoses are delayed, albeit with great effort. The corrosive effects caused by saliva, gastric juices, and bacteria can create havoc with normal tissues, so the passing hours and even minutes are critical. Yet with intensive care and techniques that exclude the esophagus from the normal digestive mechanisms, patients who have somehow survived weeks of perforation can be saved. The best results, though, are repairs made within a few hours of injury.

Whenever we save someone with a ruptured esophagus, we must give a nod not only to Boerhaave, but also to his brave if indulgent aristocrat, the grand admiral of the Dutch fleet whose "atrocious illness" stimulated one of history's most important clinical descriptions and started the tradition of clinicopathological conferences. Boerhaave may have failed to save his patient, but the baron did not die in vain. The vividness with which his famous physician recorded his life—and agonizing death—helped imprint the mysterious ailment on the minds of centuries of healers—and at least one sharp-witted pubkeep. ■

Anthony S. Patton '58 is a retired thoracic and vascular surgeon whose career was centered at Salem Hospital in Massachusetts.



Mystery



For more than a century,
Harvard physicians have stepped into
the clinical sleuthing arena to test
their wits against some of medicine's
most perplexing cases.

RICHARD CABOT WAS IRKED; LEAFING THROUGH OLD PATIENT records, he had stumbled across a case in which the sole clinical diagnosis listed was neurasthenia—a psychiatric disorder—and yet the record concluded with a note that the patient had died and an autopsy had been performed. Considered by some a “contender to sainthood,” Cabot, Class of 1892, nonetheless saw the record as an affront to his scrupulous insistence upon scientific precision.

by BEVERLY BALLARO

Theater



MAKING A CASE: Richard Cabot's insistence on exacting scientific analysis helped give rise to the clinicopathological conference.

Cabot knew from his experience as an attending physician at Massachusetts General Hospital (MGH), beginning in 1908, that, for the most part, his colleagues on the wards did not share his meticulous propensities. It was not uncommon, in the early part of the twentieth century, for clinicians to pay scant attention to autopsy reports on deceased patients, and thus to remain ignorant of the accuracy of their official diagnoses.

His consternation at "this curious blunder" immediately inspired Cabot to dig up the postmortem record. "I found," Cabot later wrote, "that the patient had died of cancer of the pleura, but had had neurasthenic symptoms and vague intercostal pain, which had misled the clinicians." Cabot seized upon this incident and others like it as a teaching opportunity. In 1910 he began presenting diagnostic riddles at weekly meetings with house officers and visiting doctors.

These exercises ultimately evolved into MGH's ongoing tradition of clinicopathological conferences (CPCs) in which a guest physician—who receives a case summary four to six weeks in advance—is asked to deduce, before an audience of colleagues, the diagnosis of an anonymous, actual MGH patient based solely on the medical history and preliminary test results.

The CPCs became a popular weekly staple to which, as the late Franz Ingelfinger '36 once wrote, "staff and students flocked to hear discussor and pathologist engage in pedagogy, histrionics, and skillful feints, attacks, and retreats." Beginning in 1915 Cabot arranged for a stenographer to record the discussions so that any requesting physician could obtain a copy, and in 1924, the Case Records of the Massachusetts General Hospital began to appear regularly in what eventually became *The New England Journal of Medicine*, a publishing tradition that endures today.

Serendipitous Encounters

Although Cabot formalized the case method of teaching at HMS in 1900 when he made it part of the curriculum for third-year students, he was not the method's only advocate at the School. While still a medical student, Walter Cannon, Class of 1900, later the George Higginson Professor of Physiology, made a detailed proposal that gained the support of Harvard President Charles Eliot for such an approach to medical education.

Cannon had a roommate who was studying at Harvard Law School, where the legal case history method had been used since the 1870s. Envious of the gusto with which the roommate tackled his subject,

“Staff and students flocked to hear discussers and pathologist engage in histrionics, skillful feints, attacks, and retreats.”

Cannon became convinced that in-depth examinations of actual hospital records would enliven the lecture-based medical educational process, which he found unbearably dull. Cannon's intuition proved correct; by the 1930s, hospitals throughout the world were imitating the CPC format.

In the early decades of the CPCs, physicians pitted their skills as general diagnosticians in an arena in which exchanges sometimes grew testy. “An occasional discusser has been accused of CPC-manship in quest of the correct diagnosis,” noted a former editor of the CPCs, Robert Scully '44, acknowledging that “discussion of the case records as unknowns introduced a challenge and, at times, a measure of discomfort for the speaker as well as zestful competition on the part of those students and physicians in the audience who chose to participate.”

In 1960, another editor of the CPCs, Benjamin Castleman, tried to quash this impulse. Castleman took pains to emphasize the value of the CPCs as “an exercise in deductive reasoning and clinicopathological correlation,” opining pointedly—and largely on deaf ears—that “it is less important to pinpoint the correct diagnosis than to present a logical and instructive analysis of pertinent conditions involved.”

The Body Eclectic

Those “pertinent conditions” invited narrow scrutiny at first; Cabot himself analyzed most of the early cases—so much so that, for many years, physicians commonly referred to the CPCs as the “Cabot Cases.” But as time went on, Cabot began to invite generalists and specialists from within MGH and from other Boston hospitals to take up the challenge.

Unlike physicians of an earlier century, who often ascribed illness to vague theories of imbalances, the disease detectives of Cabot's era focused on pinpointing organic cause-and-effect. In a 1933 case, for example, Cabot exhorted his audience to consider all the possible rational explanations for the swollen right eyelid—preceded by severe heartburn, muscle pain, nausea, and vomiting—that had brought a 32-year-old Armenian housewife, with a habit of eating lightly cooked sausage, to MGH for treatment.

Cabot began by responding to the initial report, which stated that the woman had been ill with “all the typical grippé symptoms” for a week. “Of course,” Cabot grumbled, “there is no such thing as ‘typical grippé symptoms.’...In general if we see people with

swollen eyelids and we don't know why, what unusual diseases do we think of?” Delighted by a student's response of trichinosis, Cabot enthused, “Yes. You may go a lifetime and not see a case, and then if you do see one and recognize it you are *the* person in that town or village for a time, because nobody else will think of it.”

And yet Cabot's satisfaction at receiving confirmation of his hypothesis—by a biopsied piece of the patient's muscle riddled with unencapsulated worms—was sobered, as it often was in his day, by the reality of limited options. “Of course there is no treatment in this disease,” Cabot went on to say. “We just wait for nature to cure. Death is very rare.”

Stranger than Fiction

The case indices of the 1950s and 1960s, include, as in earlier decades, a high incidence of CPCs devoted to cancer and cardiovascular disease. But they also began to explore less common conditions such as Marfan syndrome and Wegener's granulomatosis. This trend only intensified during the 1970s and 1980s.

A curious 1984 case, for example, centered around the pain and swelling in the left forearm of a 39-year-old Florida man who had traveled to New England. Doctors quickly established that gas in the tissue of his forearm, to which he had suffered a gunshot wound some 17 years earlier, was the source of the man's discomfort.

Initial concerns focused on the man's occupation as a shrimper; commercial fishermen, the presenter pointed out, face a risk for cellulitis from various sea organisms as well as other hazards of their trade: “If...this patient had been bitten by a seal,” the presenter noted, “so-called seal finger would have been included in the differential diagnosis.” But the lack of systemic toxicity and the patient's confusing history deepened the mystery—and the doctors' suspicions.

Two different hospitals in which the shrimper claimed to have been treated could find no record of him. When more checking revealed that the man went by several false identities, the diagnostic trail shifted to psychiatry. The gas in the patient's arm tissue, the presenter concluded, was there because the man had deliberately injected air into his own arm. In a bid for attention, he had engineered his own symptoms, the desperate act of a patient in the throes of Munchausen syndrome.



CANNON FODDER: Walter Cannon sought to enliven medical education by supplementing dull lectures with the analysis of actual patient cases.

Unusual Suspects

Throughout their history, the CPCs have mirrored changes not only in the science of medicine but also in the increasingly specialized medical profession and in society at large. In the 1980s and 1990s, as genetics came to assume more and more importance in the understanding of disease, and as international travel increasingly transformed previously localized outbreaks of illness into potentially global concerns, the content of the CPCs shifted in response: presenters from these years wrangled with such cases as incontinentia pigmenti—a rare genetic disease of the skin, hair, teeth, and central nervous system—and Dengue hemorrhagic fever, a flu-like viral illness spread by the bite of infected mosquitoes, common in most tropical regions of the world.

In another reflection of changing times, irresolvable diagnostic puzzles became increasingly scarce. But when such riddles did come up at the CPCs, presenters sometimes proved ominously prescient. By the early 1980s, discussers were puzzling their way through what would eventually be identified as AIDS-related diseases. Discussing the unlikely 1982 case of a 29-year-old patient with Kaposi's sarcoma—a form of skin cancer until then seen primarily in elderly Italian and Jewish men—the presenter noted that his diagnosis “should be placed in the context of an emergence of a series of remarkable observations concerning diseases among homosexual men.

“The major unanswered question, which looms over this entire discussion,” he worried, “is what accounts

for this extraordinary cluster of cases of Kaposi's sarcoma and opportunistic pathogens in this population. Are we dealing with activation of a latent agent that induces immunosuppression that itself has pluripotential expressions of disease?”

In more recent years, presenters methodically combing through patients' histories for clues have arrived at diagnostic deductions that technology alone failed to yield. A brain lesion, for example, in a researcher was linked not to the man's work experience on a HIV vaccine trial in East Africa, as first feared, but rather to schistosomiasis, a disease caused by

parasitic worms found in Lake Victoria, where the researcher had unwisely chosen to swim.

In another case, a toxic reaction in a young man, carried incoherent and incontinent into the emergency department after a round of drinking, was connected to the man's attempt to heighten alcohol's effects by gulping down cleaning fluid intended for laser printer toner cartridges.

Yet another case traced a painful shin bone infection in a liver transplant recipient to an inhalation of *Cryptococcus neoformans*, which the man's weakened immune system could not stop from disseminating to the skin and bone of his leg. This yeast-like fungus is ubiquitous in nature, the discussor noted, because it characteristically inhabits soil contaminated by pigeon feces or the debris that surrounds pigeon roosts. The patient, who enjoyed cultivating roses, had come into contact with soil that, the presenter theorized, was most likely the origin of his terrible infection.

Ghosts of Litmus Past

When the current editor of the CPCs, pathologist Nancy Harris, took over the position in 2003, she conceded that “changes in the practice of medicine mean that cases involving diagnostic mysteries suitable for the traditional CPCs are becoming more esoteric and less relevant to practice.” Yet, in her view, an updated version of Cabot's original vision of using real patient cases to teach physicians remains as valuable as ever.

An Indonesian teenager was treated after she survived a 65-foot-high wall of water, mud, and debris.

While Harris has retained the classic diagnostic-mystery format in some cases, many others contain both differential-diagnosis and management components, with an emphasis on prevention, diagnosis, prognosis, or therapy. In their new form, the CPCs' rarified—yet profoundly pragmatic—ethos endures. In one recent case, an Indonesian teenager was treated by volunteer MGH physicians aboard the USNS *Mercy* after she survived a 65-foot-high wall of water, mud, and debris that devastated her hometown of Banda Aceh. The December 2004 tsunami had swept the girl more than a mile inland, nearly drowning her, and claimed the life of her mother, whose body was never recovered.

The CPC at which the girl's case was presented to a packed amphitheater was a far cry from the conferences of Cabot's era; an array of specialists armed with the latest databases of knowledge in pediatrics, neurology, and infectious diseases solved the mystery of the girl's symptoms deftly and decisively—and with the live participation, via videoconferencing satellite connection, of physicians on board the

Mercy, afloat in the Indian Ocean, thousands of miles and multiple time zones removed from MGH.

And yet, for all its cutting-edge quality, this CPC reverberated with an echo of the tradition's original spirit. In the absence, on the ship, of some of the highly refined diagnostic technology to which physicians have routine access at MGH, some of the presenters recounted the roles that improvisation, deduction, and intuition had played in helping them to arrive at a successful diagnosis and treatment. The elegance—and compassion—with which the MGH physicians presented the Indonesian teenager's case would have gratified Cabot, who, despite being a staunch champion of the emerging biosciences of his time, never lost sight of the human stakes at the center of the CPCs. After all, Cabot wrote in his later years, "I was not interested in Disease but rather in spotting it and getting people over it." ■

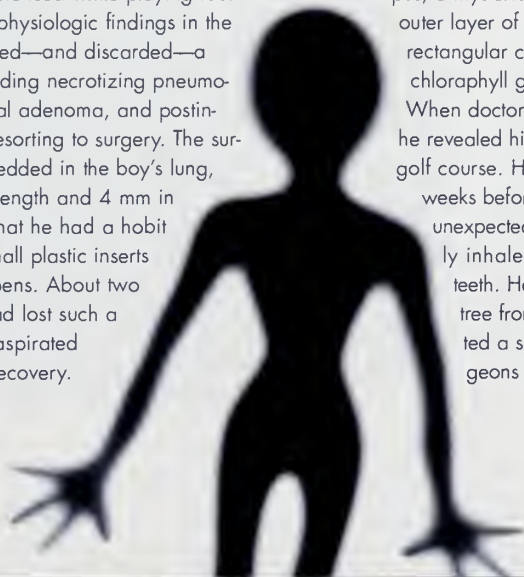
Beverly Ballaro is associate editor of the Harvard Medical Alumni Bulletin.

Alien Invaders

The database of the thousands of CPCs that have been presented since the early 1920s can be searched according to various terms such as "diagnosis" and "organ involved." As the following cases illustrate, some of the most unusual puzzles—even by CPC standards—can be retrieved under "foreign objects."

When a 14-year-old boy was admitted to MGH because he had been coughing up blood, for example, suspicions initially centered on a blow to the chest he had experienced while playing football. Yet after x-rays revealed pathophysiologic findings in the boy's lungs, the physicians considered—and discarded—a number of possible diagnoses, including necrotizing pneumonia, measles pneumonia, a bronchial adenoma, and postinfectious bronchial stenosis, before resorting to surgery. The surgeon's explorations turned up, embedded in the boy's lung, "a blue plastic cylinder, 12 mm in length and 4 mm in diameter." The boy later admitted that he had a habit of removing and chewing on the small plastic inserts used to plug the ends of ballpoint pens. About two years earlier, while doing so, he had lost such a piece. The surgical removal of the aspirated object led to the youth's complete recovery.

In another case, the prospects looked grim for a 75-year-old man admitted for chest pain and a bloody cough. When CT scans revealed a mass in the lungs, doctors suspected that the man was suffering from a primary cancer. Although he had quit smoking 40 years earlier, his wife had continued her habit, exposing him to decades of secondhand smoke. But a subsequent resection of the lung tissue in question turned up not a malignant tumor but a fragmented foreign body immersed in pus, a mysterious item consisting of "a continuous, birefringent outer layer of cellulose and an inner thick layer composed of rectangular cells with thick walls, central phloem tubes, and chlorophyll granules"—in layman's terms, a sprig of plant. When doctors reported their curious findings to the patient, he revealed his habit of chewing grass and twigs while on the golf course. He recalled one episode in particular, about six weeks before his symptoms had begun, in which someone's unexpected approach had startled him and he had suddenly inhaled the piece of evergreen poked between his teeth. He later returned to the golf course, identified the tree from which he had broken off a piece, and submitted a sample for laboratory comparison with what surgeons had excised from his lungs—a perfect match. ■

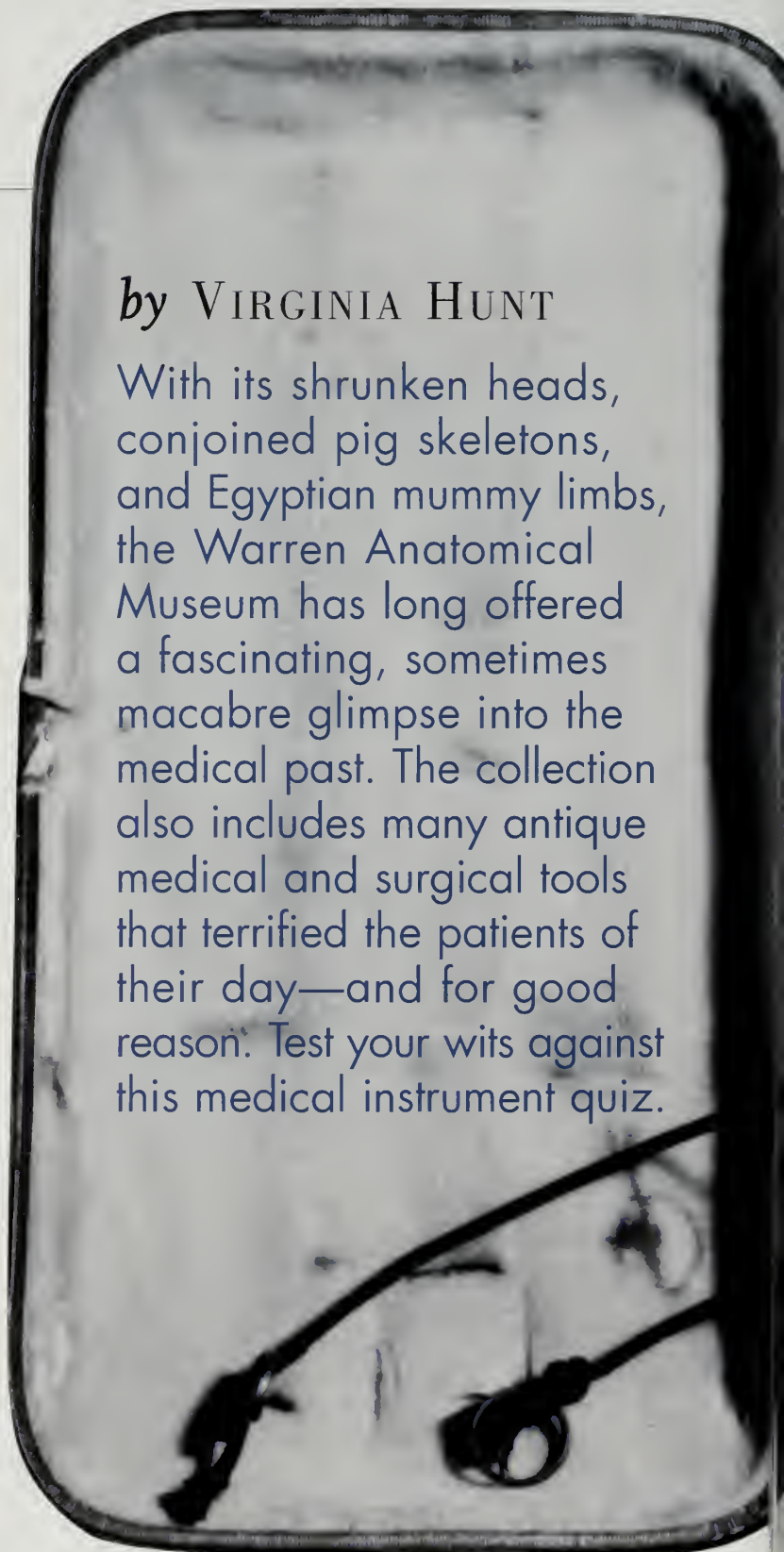


name
that

Tool

by VIRGINIA HUNT

With its shrunken heads, conjoined pig skeletons, and Egyptian mummy limbs, the Warren Anatomical Museum has long offered a fascinating, sometimes macabre glimpse into the medical past. The collection also includes many antique medical and surgical tools that terrified the patients of their day—and for good reason. Test your wits against this medical instrument quiz.





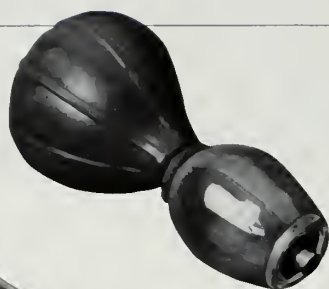
1

- A. Blood transfusion kit
- B. Urethral syringe set
- C. Artificial leech
- D. Enema pump

C. Artificial Leech, ca. 1865

Invented by Baron Charles Louis Heurteloup in the 1840s, the artificial leech served “overly sensitive” patients who turned squeamish at the prospect of living creatures sucking on their skin. Especially popular for bleeding the temples to treat eye afflictions, mechanical leeches functioned the same way as their insect-world counterparts. The device consisted of a pointed lancet stored inside a glass syringe cylinder, or “sucker.” The 3,000-year-old practice of bloodletting reached its zenith at the beginning of the nineteenth century. According to its advocates, the process drained poisons or excess blood from the body, thus restoring the balance of the humors. Today some doctors continue to use real leeches to restore circulation, particularly after microsurgery.

Over time the postoperative death rate the number of successful cases



2.

- A. Ether administration tools
- B. Lithotripsy and litholopaxy instruments
- C. Embalming cavity injection kit
- D. Fleam with fleam stick

B. Lithotripsy and litholopaxy instruments, ca. 1871

Physicians have treated bladder stones both medically and surgically for many centuries. In the early 1800s, lithotomy, or the process of crushing the stones to facilitate their passage, became the preferred treatment because it avoided the need for incisions. Many lithotomies resulted in cystitis infections, however, and—given the lack of anesthesia and high death rate—patients dreaded the operation. Henry Jacob Bigelow, professor of surgery at Harvard Medical School, sought to create a procedure that immediately removed the crushed stone fragments from the body, thus reducing the potential for a deadly infection. To do this, he flushed the bladder with water through a urethral tube, a process he dubbed “litholopaxy.” Over time the postoperative death rate declined and the number of successful cases increased.

3.

- A. Scarificator
- B. Medicine bottle opener
- C. Scalpel sharpener
- D. Trocar

A. Octagonal Brass Scarificator, Mid-Nineteenth Century

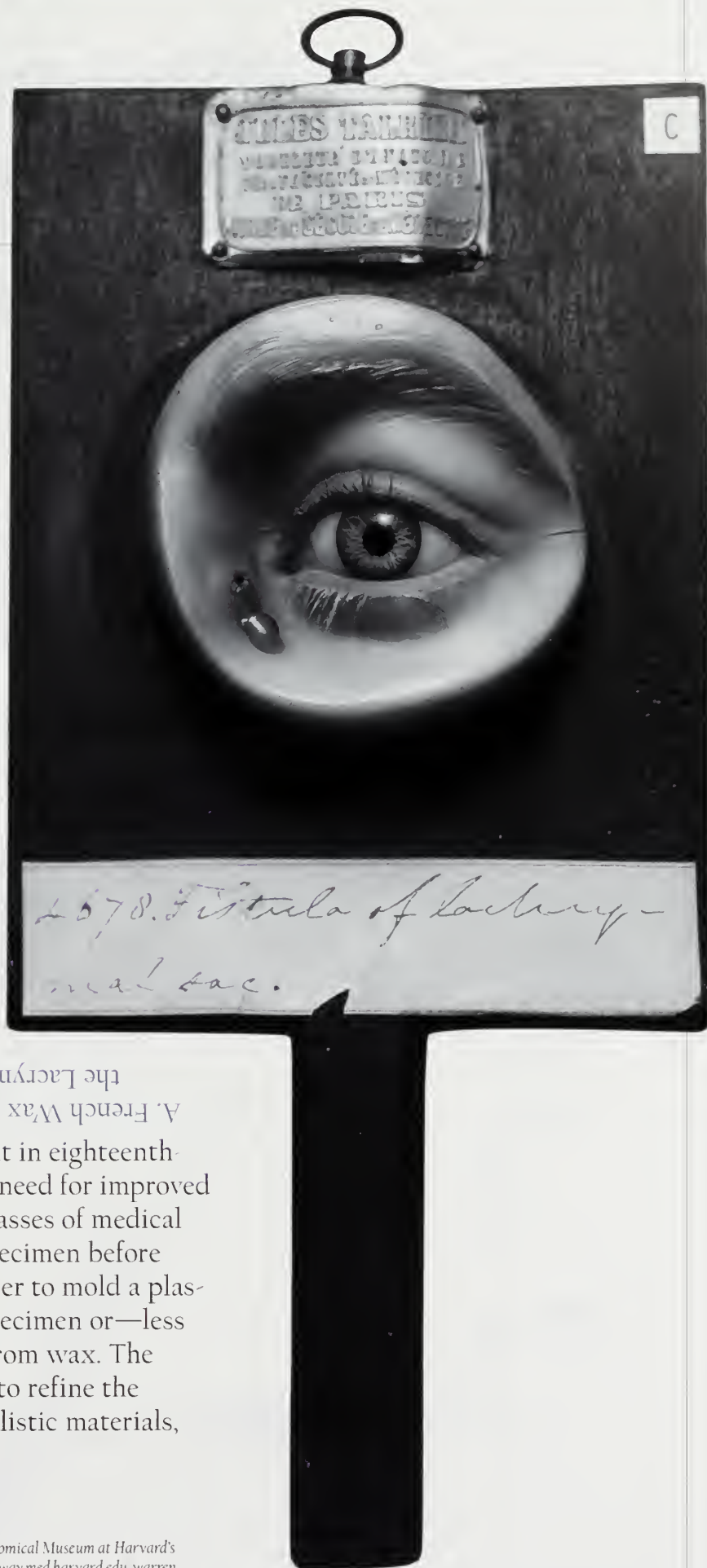
From the time of the ancient Egyptians and into the twentieth century, healers turned to bloodletting to relieve such maladies as epilepsy, tuberculosis, intoxication, and hydrocephalus. The scarificator was considered more humane than other instruments used to gain access to the blood. The device consisted of a dozen spring-driven rotary blades that produced multiple shallow cuts when the bloodletter uncocked the trigger.



declined and increased.

4.

- A. Wax eye model
- B. Psychological test card
- C. Ophthalmophantome
- D. Demonstration showcase for prosthetic glass eyes



A. French Wax Eye Model Depicting a Fistula of the Lacrymal Sac, Early Twentieth Century

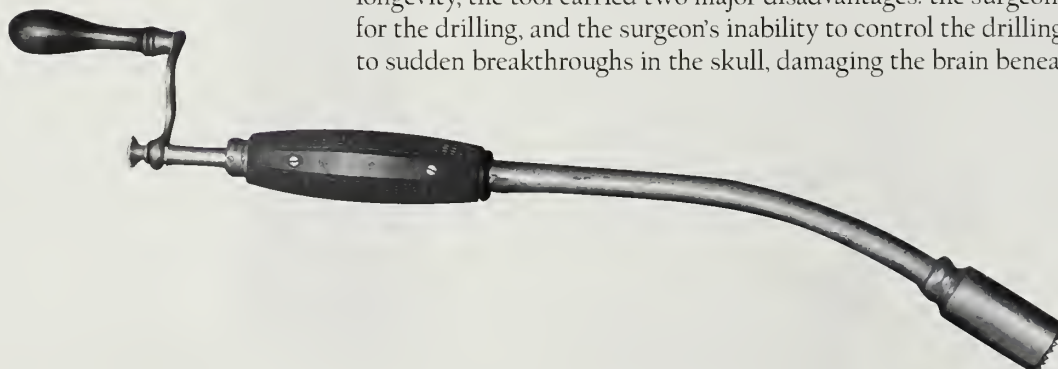
Wax modeling reached its height in eighteenth-century Italy in response to the need for improved visual aids for teaching larger classes of medical students. With the dissected specimen before him, the modeler decided whether to mold a plaster negative directly from the specimen or—less commonly—to sculpt a model from wax. The modeler then used heated tools to refine the model, painted it, and added realistic materials, such as eyelashes.

Virginia Hunt is the curatorial assistant for the Warren Anatomical Museum at Harvard's Francis A. Countway Library of Medicine. Visit www.countway.med.harvard.edu/warren to learn more about the museum.

Practitioners often of forceps that

- A. Tonsilotome
- B. Archimedes dental drill
- C. Trepan
- D. Bistoury cachet

5.



C. Trepan, ca. 1860s

Trephination—or trepanation—involves drilling or scraping a hole into the skull, leaving the membrane surrounding the brain intact. This surgical procedure is reflected in prehistoric human remains and documented in cave paintings. Anthropologists have theorized that by opening a hole in a sick person's skull, ancient surgeons believed they could release the demonic spirits causing the illness. In later eras, doctors used the procedure to relieve intracranial pressure and to facilitate the elevation of depressed skull fragments. By the seventeenth century, craftsmen were creating specialized surgical kits aimed at making drilling easier and preventing the blades from penetrating too deeply. The first editions of the design pictured here—which persisted into the twentieth century—appeared in the 1560s. Despite its longevity, the tool carried two major disadvantages: the surgeon needed both hands for the drilling, and the surgeon's inability to control the drilling pressure could lead to sudden breakthroughs in the skull, damaging the brain beneath.

extracted teeth with the same kind coopers used to fit hoops on barrels.

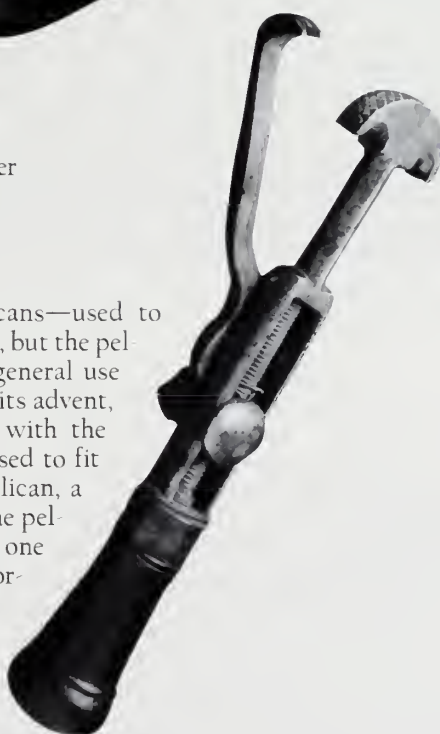


6.

- A. Toothkey
- B. Pain obturator
- C. Gingival trimmer
- D. Dental pelican

D. Dental Pelican, ca. 1750

The first reference to dental pelicans—used to extract diseased teeth—dates to 1363, but the pelican is believed to have come into general use during the sixteenth century. Before its advent, practitioners often extracted teeth with the same kind of forceps that coopers used to fit hoops on barrels. In this style of pelican, a central screw mechanism adjusted the pelican's width. Instruments like this one eventually fell out of use in favor of forceps-style pelicans and toothkeys.



7.

- A. Amalgam carver
- B. Obstetrical forceps
- C. Tarnier's basiotribe
- D. Arrow remover

ca. 1753

B. Obstetrical Forceps,

Peter Chamberlen the Elder, a barber surgeon, invented the obstetrical forceps at the turn of the seventeenth century, but a desire to profit exclusively from its use drove his descendants to keep the design a secret for 125 years. In the 1740s William Smellie, a Scottish obstetrician, began experimenting with new designs similar to this pair, which was fenestrated and covered with leather. Smellie insisted that the leather be replaced after each delivery to avoid venereal infection—a view that predated positing by Oliver Wendell Holmes, Class of 1836, that the puerperal fever that led to so many postpartum deaths was spread from patient to patient by the physicians and midwives delivering the babies.



The Bearable Lightness of Being

HE NEEDED TO ESCAPE—FAST—BUT BOBBY SATCHER '94 FELT disoriented. Upside-down and in darkness, he couldn't recognize the familiar landmarks—a windowsill, the edge of a seat—that would help him find his way out. Water rushed into the cockpit with a *whoosh*, distracting him. Sweating in a full flight suit and helmet, Satcher tried to follow his evacuation

plan methodically. He had no oxygen mask, though, and knew he had only six seconds—tops—before water completely flooded his remaining air space. He couldn't orient himself, so he skipped to the next steps in his plan. Those harrowing few moments, he later recalled, were some of the hardest in his training, but he finally managed to free himself without rescue from the divers stationed nearby.

Satcher was in the "helo-dunker"—a simulated, sinking helicopter cockpit in the pool at the Naval Air Station in Pensacola, Florida, as part of his training to be an astronaut. "Planes are top-heavy, so the cockpit flips upside-down and sinks," he explains. "The helo-dunker prepares you for such an event. It's safe and *thoroughly* scary. It makes you confront your fears."

In June 2004, Satcher began 18 months of basic training, which includes airtime in jets, water and wilderness survival in case of a crash, team-building exercises, physical conditioning, and sessions in NASA's Neutral Buoyancy Laboratory.

Thus far he has survived a series of simulated crises and a bookcase of reading. "The program reminds me of my first two years at HMS," he says. "You have so much information to process. My manuals stack up four feet high."

This time, though, Satcher's "class" consists of only ten others. He is a mission specialist—what he calls a proxy scientist—which means during space flight he will likely conduct physical science and medical experiments designed by other researchers. Before moving to Houston to begin astronaut training, Satcher's own research focused on how bone cells

sinking cockpit, some of his best moments have also occurred in cockpits—flying the Air Force's supersonic jet trainers, the T-38 and the KC-135. "G-forces load on you in high-performance jets," he says. "You feel like you're being mashed down in your seat. If you experience four Gs, your fingers weigh four times more than normal, making it harder to move your hands." Wearing an oxygen mask in the T-38, he crews for the pilot as navigator and communicator, manning the onboard computer and radio navigation aids.

In the KC-135—nicknamed the "vomit comet" for its stomach-dropping, loop-de-loop flight—he experiences 30 seconds of weightlessness at the top of each parabolic arc—a blip that resembles space travel. "You're just floating," he says. "You can feel all the stress and strains on your body disappear. Instruments in your hands float away, and you can do flips and spins in the air. It's part physics lesson, part fun." He and his fellow trainees can zoom around the padded cabin with just a slight push off a wall.

Satcher wishes he could have gained such relief after performing surgery. "I often did operations that lasted 12 to 14 hours," he says. "Afterward, my shoulders ached and my back felt cramped—it would have been great to have been able to enter a



THAT SINKING FEELING: Orthopedic surgeon Bobby Satcher, an astronaut-in-training, suits up for water survival practice in the "helo-dunker" in Pensacola, Florida.

respond to changes in gravity and how the skeleton remodels itself. He also practiced orthopedic surgery at Northwestern Memorial Hospital and taught orthopedics at Northwestern University's Feinberg School of Medicine.

Although Satcher's most frightening moments thus far were those in that

zero-gravity situation."

To challenge Satcher's class with a different kind of gravity, NASA deposited Satcher and his peers in some woods in western Maine for four days of wilderness survival training. In crisp, 40-degree weather, they slept on rain ponchos in "hootches" made from para-

chute fabric. Although they had received briefings on insects and wildlife they could safely eat, Satcher chose not to supplement his meager rations. "The iodine-flavored water tasted bad enough," he says. During the final exam, instructors watched as each team rescued an injured trainee and humped their heavy gear out of the forest. "The whole point," Satcher says, "is to execute a plan under tough circumstances."

Satcher has a knack for creating tough circumstances for himself and then overcoming them. While at HMS, he also earned a doctorate in chemical engineering at MIT. But his dream of becoming an astronaut hatched early. "I started thinking about it as a kid, the same as any kid," Satcher says. His mother, an English professor, and his father, a chemist and college professor, never pushed him in any one direction, he says, but they encouraged his interest in math and science. Satcher avidly followed the space program while in college and at HMS. Becoming an astronaut didn't seem possible, though, until he met some people from NASA during his residency. "Once I started learning about astronaut training," he says, "I knew it was for me."

NASA agreed. Satcher's research on how external forces affect the skeleton appealed to those running the agency's new Vision for Space Exploration program, as they hope to study the effects of long-duration space flight on astronaut health. Satcher launched the formal application process while starting his family, and NASA chose him as one of a hundred candidates to brave the week-long battery of interviews. His first child arrived the same day as the news of his acceptance into NASA's program, adding two new challenges and two new titles to his growing list.

As a parent, Satcher is even more aware of the dangers of space travel. "It's a job with well-publicized but not unacceptable risks," he says. "Managing those risks is the highest priority for NASA. My



"G-forces load on you in high-performance jets. You feel like you're being mashed down in your seat. If you experience four Gs, your fingers weigh four times more than normal, making it harder to move your hands."

family members are supportive of my dream, though they have their concerns."

An astronaut's work is physically demanding, Satcher adds. "Space is a harsh environment. Radiation, microgravity, and confined quarters take their toll on the body. And outside the ship, we have to learn to maneuver in a space suit, which is not the most natural feeling."

This summer, Satcher will be dunked in water once again and learn to maneuver in a suit—this time in NASA's Neutral Buoyancy Laboratory, a 40-foot-deep indoor pool, big enough to house mock-up components of the International Space Station. Neutral buoyancy is not quite zero gravity because astronauts still feel their weight, but it comes close. Satcher will spend seven hours at a time under-

water, practicing "extravehicular activities," such as testing new flight tools, operating hydraulic robots to repair the station's components, and walking in conditions that mimic space.

Satcher predicts he'll wait several years before going on a mission because the suspension of space shuttle flights following the *Columbia* tragedy in February 2003 created a backlog of qualified astronauts. That backlog may soon begin to dissipate, however; NASA anticipates sending astronauts into orbit once again, as early as this summer.

For Bobby Satcher, the future looks buoyant. ■

Janice O'Leary is assistant editor of the Harvard Medical Alumni Bulletin.

SPACE CADET: Astronaut-in-training Bobby Satcher '94 floats in the cabin of the "Weightless Wonder," a high-performance KC-135 jet that NASA uses to introduce trainees to zero gravity.



Harvard Medical Alumni Association
25 Shattuck Street
Boston, Massachusetts 02115
Change Service Requested

Non-Profit Organization
U.S. Postage PAID
Permit No. 52420
Boston, MA

PHOTO COURTESY OF NASA